"PRE CLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM*** (EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU)"

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled “Pre clinical and comparative clinical trial of Siddha drugs ***Parangipattai Kudineer*** (Internally) and ***Sivappu Thylam*** (Externally) in the treatment of ***Kalanjagapadai*** (Psoriasis) with and without Yogam therapy (Agathavam Ettu)” is a bonafide and genuine research work carried out by me under the guidance of **Dr.M.V.Mahadevan,M.D(s),Ph.D,** Lecturer**,** Department of Sirappu Maruthuvam, National Institute of Siddha, Chennai -47, and the dissertation has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

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BONAFIDE CERTIFICATE

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1.INTRODUCTION :

Siddha system is one of the ancient science of our nation with an almost unbroken tradition of safety and efficacy. Siddha system of medicine considers human beings in their totality and their subtle relationship with the universe. The beauty of this system is that it doesn't look at health as being merely the absence of disease, but in positive terms of balance and harmony of body, mind,soul.

"Elements of macrocosm exists in microcosm
Elements of microcosm exists in macrocosm
Macrocosm and microcosm are one
When realization is complete"

- ***Chattamuni Gnanam[1].***

The human powers and the natural powers are responsible for the functions of the universe, which are neither different nor variant in nature. The Siddhars explained all body functions relative to the happenings in the universe.The body is made up of *Udal thathus* (physical constituents), *Uyir thathus* (biological humors).If the inherent powers within the human beings, such as the *Mukkunam,Mukkutram, Udal thathukal, Kosam* and *Aadharam* act against the natural powers to generate the diseases. [1]

Noi or disease is the state arising from inability of bodily nature to meet with or neutralize the increased or morbid effects resulting from the varied changes taking place in the system. It is known as *pini,varutham,thunbam,vinai,rogam and sugaveenam.*[2]

The skin diseases are classified into *18* varieties by *Siddhar Yugi Munivar.* One such skin disease is *Kalanjagapadai.* The symptoms of *Kalanjagapadai* can be correlated to those of the clinical entity Psoriasis in modern system of medicine. He has described under the classification of vaatha diseases about *"Kalanjagavatham"* which may be correlated with Psoriatic arthropathy.[3]

In the textbook *"Siddha Maruthuvam Sirappu",* Dr.R.Thiagarajan has described about Kalanjagapadai. The clinical features of Kalanjagapadai are correlated to psoriasis as described in modern dermatology. In the Siddha system, skin disorders are brought under the clinical entity *"Kuttam".*

Psoriasis is common, chronic skin disease, affecting approximately 2% of the population. Psoriasis is associated with a high degree of morbidity ; patients are embarrassed about the appearance of their skin,and there side effects of medications.In addition, patients

with psoriasis have reduced levels of employment and income as well as a decreased quality of life.[4] The prevalence of psoriasis to be 0.44% to 2.8% among the skin patients in India. Highest incidence was noted in the age group of 20-39 years and the mean age of onset is males and females were comparable.[5]

The exact cause of psoriasis remains unknown. There may be a combination of elements, including genetic predisposition, environmental factors, stress also a trigger for a psoriasis flare. Psoriasis independently associated with stress related disorders.[6]

The Siddha system approaches diseases by holistic way to prevent and treat the condition. Hence the proper assessment of disease through various diagnostic tools mentioned in siddha literatures and with modern scientific methods.

The number of *Kalanjagapadai* patients attending the National Institute of Siddha hospital is considerably increasing day by day. Patient is very much agitated and subjected to physical and mental suffering. However encouraging results are obtained in our Siddha system. With this back ground the disease *Kalanjagapadai* was chosen for the dissertation study.

However clinical symptoms can be relieved considerably with Siddha treatment.Siddhars identified numerous number of herbal for treating psoriasis. One such Siddha herbal formulation ***"Parangipattai Kudineer"*** **(Internal) and** ***"Sivappu Thylam"*** **(External)** mentioned in "Pharmacopoeia of hospital of Indian medicine" which is said to be efficacious and simple formulation. This formulation has not undergone any clinical trial so the investigator has selected the above drugs.

2.AIM AND OBJECTIVES

2.1.PRIMARY OBJECTIVES :

To evaluate the safety and therapeutic efficacy of Siddha drugs, ***Parangipattai kudineer (Internally)*** and ***Sivappu Thylam (Externally)*** in the treatment of *Kalanjagapadai* (Psoriasis)

2.2.SECONDARY OBJECTIVES :

- To studied the Siddha diagnostic methods such as ***Envagai thervu , Manikkadai Nool, Neer kuri and Nei kuri*** as complementary measures for diagnosis in *Kalanjagapadai* patients.
- To carried out the **biochemical analysis** of trail medicine *Parangipattai kudineer* (Internally)
- To carried out **analytical specification** of a trail medicine *Parangipattai kudineer* chooranam (Internally) as per **AYUSH protocol**.
- To evaluated the ***acute and sub-acute toxicity*** of the trial drug as per **OECD** guidelines.
- To evaluated of pharmacological activities ***(In-vitro:Anti-Inflammatory, Immunomodulator, Anti-proliferative)*** of trail medicine ***Parangipattai kudineer*** **chooranam (Internally)**
- To evaluated of **docking analysis** of trail medicine ***Parangipattai kudineer*** **chooranam (Internally)**
- To evaluated of ***In-vitro anti-inflammatory*** activities of trail medicine ***Sivappu thylam*** **(Externaly)**
- To collected a detailed of literatures of trial drug and the disease *"Kalanjagapadai"* and review the ideas mentioned in siddha literatures related to this disease.
- To studied the effectiveness of Yogam along with medicine in kalanjagapadai IPD patients.
- To made a detailed clinical evaluation of the disease by examination on aetiology,symptomology,complication, treatment,and prognosis.
- To studied the incidence of *"Kalanjagapadai"* with reference to age, sex, family history, occupation, socio-economic status , habit,and also related to psychosomatic problems, seasonal variance ,udal thathus,uyir thathus, etc.,

3.REVIEW OF LITERATURE

3a.SIDDHA ASPECT

3a.1.KALANJAGAPADAI

3a.1.1.SYNONYMS :

Venparu sedhil, Sedhiludhir noi,Sambal padai ,Sedhil udhirpadai[3]

3a.1.2.DEFINITION :

According to the text book of ***"Siddha Maruthuvam Sirappu"*** *Kalanjagapadai* is a chronic non-infectious,recurrent, inflammatory disorder of the skin characterized by,reddish , slightly elevated dry patches covered with silvery white scales.In Siddha system,Skin disorder are brought under the clinical entity *"Kuttam*.[7]

In the textbook **"Siddha medical dictionary"- Mr.T.V.Sambasivam pillai** has described about *"Kuttam"* means cutaneous affections and so it is a comprehensive term used for various skin diseases. In this book ***"Sori kuttam"*** has been compared to psoriasis, a kind of leprosy with diffuse papular eruption with ulceration on the entire surface of the body marked by intense itching and burning sensation followed by exfoliation of the epidermis or browny scales (Eczematous psoriasis, lepra icthyosis).

In the text book ***"Aathma Ratchamirtham ennum Vaithiya saarasangiragam"*** the characteristics of *kuttam* are described as; white scaly patches will appear in foot, wrist and typical extensor distribution.

3a.1.3.FACTS OF SKIN DISEASES:

It is a disease believed due to a reflection of one's previous births (karma).

Some authors of Indian medical science attribute the origin of this disease to several pathological causes such as venereal diseases,syphilis, ring worm, snake bite , poisonous insects bite or sting,infection,inheritance.

3a.1.4.AETIOLOGY :

"வாதமலாது மேனி கெடாது"

- தேரன் சேகரப்பா[8]

தேகத்தின் ஒளியும் வன்மையும் கெடுவதற்க்கு வளிக்குற்றமே முதற்காரணமாகும்.

The Siddha literatures explain the aetiology, clinical features of *Kuttam* have been mentioned in below ;

The text book ***Siddha Maruthuvam Sirappu,***

- Unknown etiology
- Genetic cause

The text ***Agathiyar Paripooranam – 400*** describes the Psycho-social causes (Kanma Varalaru);

“பழவினையால் விஷப்பூச்சி கடித்த தோஷம்
பாதகர்க்கு ஒரு நாளும் தீர்வதில்லை
உளவினையா லூடாபிக் கொள்ள வந்த
உண்மையது அறியாமல்மூர்க்களுஞ் செய்வார்
களவினையுந் தீர்வதில்லை கடினமெத்த
கருணையுள்ள பூரணத்தில் கண்காட்சி
அடவினை நீகாணுமுன்னெ அகலச் சொல்லி
அடையாளம் விரல் குறுகு மின்னங்கேளே”.

“விரல்குறுகுங்கால்திமிரும் விஷம்போலேறும்
மெய்யமுந்துந் தலைசுழலும் வெளுக்கும் மேனி
பரமான தேகமெல்லாந் தடித்து வீங்கும்
பாதமெல்லாம் வெடித்துமிகப் புண்ணாங் காணும்
சரசமூடன் சொறிகரப்பான் பணம்போல் தோணும்
சந்தையாமே விந்தைகெடுந் தடித்து வீங்கும்
நரருலகி லிந்நோய்க்கு மருந்தீயாதே
நல்லோரைப் பழித்தகுட்டங்கன்மமாமே”.

In ***Agathiar Paripooranam 400*** it has been mentioned that diseases which are caused due to sins committed in the previous birth will be cured only if *Kanmam* is expiated.

Siddhar *Agathiyar* mentioned that *Kanmam* (Genetic predisposition) is the main cause for *Kuttam* in the text ***Kanma Kandam*** as follows:

“சேர்ந்த குட்டமொடு குறைநோய்கள்
சேதிகேள் மலராத வரும்ப கொய்தல்
தாரிந்த சீர் செந்து வதைகள் செய்தல்
தாய் தந்தை மனது நொந்து ரோகந்தானே
தானென்ற தெய்வவுருத் தனையழித்தல்
சார்வான பெரியோர்கள் தமைப் பழித்தல்
கானென்ற நந்தவனம் பூஞ்செடிகள் வெட்டல்
கருமமடா சரீரத்திற் காசு போலே

யூனென்ற வுடம்பெல்லாம் மொட்டு மொட்டா
யுடன் வெளுத்து குறையோயுதிரஞ் சிந்தும்
வானென்ற கருமங்கள் தீர்ப்பதற்கு
வரையொன்று சொல்வேன் கேள் நந்தவன்மையே".

- Plucking the flower buds
- Cruel to animals
- Destroying statues of god
- Abuse elderly people
- Destroying forests and gardens.

3a.1.5.SIGNS AND SYMPTOMS:

The predominant symptoms are

- Roughness of skin
- Itching sensation
- Anaesthesia of the parts
- Rapid growth and spread of ulcers.

In ***Thirumoolar Vaithiyam***

"வியாதியுள் மூவாறு விளங்கிய குட்டங்கேள்
சுயாதிக் கிரந்தி சுழல் மேகத்தா லாறும்
பயாதி மண்ணுளப் பலவண்டினா லெட்டும்
நியாதி புழுநாலாய் நின்றதிக் குட்டமே".

- Six types of skin diseases are caused by venereal disease
- Eight types of skin diseases are caused by insect bites
- Four types of skin diseases are caused by worm infestations.

In ***Guru Naadi Nool***

"கிருமியால் வந்த தோடம் பெருகவுண்டு
கேட்கி லதன் பிரிவுதனை கிரமமாகப்
புழுக்கடிபோல் காணுமது கிருமி யாலே
செருமிவரும் பவுத்திரங்கள் கிருமி யாலே
தேகமதில் சொறிக்குட்டம் கிருமி யாலே
துருமிவருஞ் சுரோணிதங் கிருமி யாலே
சூட்சமுடன் கிரிசைப்பால் தொழில்செய் வீரே".

As per ***Guru naadi nool*** text, the skin disease caused by worm infestations.

In the text ***Yugimuni 800***

“விளம்பவே மிகுந்தஉஷ் ணந்தன் னாலும்
மிகுந்த சீதளத்தாலு மழற்சி யாலும்
வளம்பவே மந்தத்தால் வாந்தி யாலும்
மகத்தான பெண்ணோடு மருவ மாலும்
கிளம்பவே கிலேங்சகள் மிகுத லாலும்
கெடியான வுரக்கங்கள டைத லாலும்
தளம்பவே மயிருகற்கள் தவிடு மண்கள்
சாதத்திற் பருகலால்மிக்குங் குஷ்டம்”.

Excessive heat and cold, laziness**,** sleep in day time, sexual indulgence, robbery etc. These habits are prominent among the factors which lower the immune mechanism of the body (*Udal vanmai*) and make the body liable to disease. Added to the above excessive intake of food items which are hard to digest, imbalanced diet, and vomiting due to indigestion, food contaminated with stone and hair, chronic mental depression, intention to spoil others, greed, abusing God and elderly people, neglecting orphans and beggars, cursing the elders would also affect the body and mind disturbing the mechanism of the body.

3a.1.6.Triggering Factors of Kalanjagapadai :

- Seasonal variations
- Stress and strain,Anxiety, Depression
- Respiratory disorders
- Allergic disorders
- Tonsillitis (*Lasuna thabitham*)
- Certain drugs (eg : Chloroquine, Polio vaccine *Thambira chendhuram*)

3a.1.7.CLASSIFICATIONS

According to ***Thiru T.V. SambasivamPillai*** there are 18 types of *Kuttam*, as listed below:

1. *Neer kuttam* - Leprosy with serous exudation
2. *Venkuttam* - White Leprosy
3. *Sori Kuttam* - Psoriasis
4. *Karunkuttam* - Black Leprosy
5. *Perumkuttam* - True Leprosy
6. *Senkuttam* - Macular Leprosy
7. *Pori kuttam* - Leprosy with Granules
8. *Viri kuttam* - Leprosy with Fissures
9. *Yeri kuttam* - Leprosy with burning sensation

10. *Viral kurai kuttam* - Lepra mutilans
11. *Sadai kuttam* - Leprosy with confluent ulcers
12. *Yaanai kuttam* - Thick skinned Leprosy
13. *Thimir kuttam* - Anesthetic Leprosy
14. *Virana kuttam* - Ulcerated Leprosy
15. *Kaai kuttam* - Nodular Leprosy
16. *Azhi kuttam* - A form with sloughing ulcers
17. *Kirumi kuttam* - Leprosy with microbes
18. *Aara kuttam* - Incurable Leprosy

According to **by *Dhanvanthri:***

"வாதபித்தச் சிலேற்பனத்தின் வாதரோகந் தானெனினும்
தீது குட்டமேழுந் தீரும் குட்டம் பதினொன்று
மோதுங் குட்டம் பதினெட்டுடன்றோய வையினுற் பவமும்
பேதக்குணமுவியாதியின்முன்பிறக்கும்குணமு முரைப்பேனே".

1. *Kabala Kuttam*
2. *Sarmeega Kuttam*
3. *Kideepa Kuttam*
4. *Mudhumba Kuttam*
5. *Visharchiga Kuttam*
6. *Mandalakira Kuttam*
7. *Aguvai Kuttam*
8. *Thathru Kuttam*
9. *Pundareegha Kuttam*
10. *Bama Kuttam*
11. *Kaghanandhi Kuttam*
12. *Sithma Kuttam*
13. *Vibadhiga Kuttam*
14. *Sadhariga Kuttam*
15. *Vispodaga Kuttam*
16. *Sarmathala Kuttam*
17. *Ven Kuttam*
18. *Alasa Kuttam*

According to **by *Yugi Muni Vaidhya Chinthamani:***

In his Siddha literature the "*Kuttam"* has been classified into 18 types,

"முத்தாகுங் குட்டந்தான் பதினெட்டுக்கும்
முனியான யூகிநான் சொல்லக் கேளாய்
புத்தாகும் புண்டரீக குட்டத் தோடு
பெருகின்ற விற்போடக குஷ்ட மாகும்
பத்தாகும் பரமகுஷ்டம் கேசர குஷ்டம்
பரிவான கர்ணகுட்டம் சிகும குட்டம்
கித்தாகுங் கிருஷ்ணகுட்ட அவுதும்பர குட்டம்
கெடியான மண்டலகுட் டமுமா மென்னே
குட்டமாம் பரப்பரிச குட்ட மொடு
குடிலமாம் விசர்ச்சீக குட்ட மாகும்
வட்டமாம் வையாதி குட்ட மோடு
மருவலாங் கிடீபகுட்டஞ் சர்ம தேவம்
திட்டமா தேத்திருக் குட்ட மோடு
சித்துமா குட்டஞ்சா காறுகுட்டம்
துட்டமாஞ் சுவேதகுட்டந் தன்னோ டொக்கச்
சுயம்பான பதினெட்டு குட்ட மாச்சே".

1. *Pundareegam* - *Padarthamarai*
2. *Virpodagam* - *Koppulaperunoi*
3. *Bamam* - *Siranguperunoi*
4. *Gajasarmam* - *Yaanaitholperunoi*
5. *Karnam* - *Kaadhuperunoi*
6. *Sikuram* - *Tholperunoi*
7. *Krishnam* - *Karuperunoi*
8. *Avudhumbaram* - *Athikkaiperunoi*
9. *Mandalam* - *Valayaperunoi*
10. *Abarisam* - *Valiperunoi*
11. *Visharchigam* - *Soriperunoi*
12. *Vibhadhigam* - *Sen kuttam*
13. *Sarmathalam* - *Tholvedippuperunoi*
14. *Kidepam* - *Pandritholperunoi*
15. *Thethuru* - *Thadippuperunoi*
16. *Sithuma* - *Naaperunoi*
17. *Sadharu* - *Puraiperunoi*
18. *Suvedham* - *Venkuttam*

According to sage *Yugi*, *Kuttam* have been classified as 7 types as per alteration of three humors

1) *Vali kuttam*
2) *Azhal kuttam*
3) *Iyya kuttam*
4) *Vali iyya kuttam*
5) *Vali azhal kuttam*
6) *Azhal iyya kuttam*
7) *Mukkutra kuttam*

According to sage Yugi, ten types of *kuttam* are curable

1) *Virpodagam*
2) *Bamam*
3) *Kaja sarmam*
4) *Kiruttinam*
5) *Avuthumbaram*
6) *Thaththuru*
7) *Siththuma*
8) *Kideebam*
9) *Sadharu*
10) *Sarumam*

According to sage Yugi, eight types of *kuttam* are uncurable

1) *Pundareegam*
2) *Karanam*
3) *Siguram*
4) *Mandalam*
5) *Abarisam*
6) *Vasarchigam*
7) *Vibathigam*
8) *Suvetham*

The clinical features of ***Virpodaga kuttam, Sadharu kuttam*** are resemble as ***Kalanjagapadai*.**

3a.1.8.Clinical Features

விற்போடகக் குட்டம்[7]:

"புதுமையாய்ச் சரீரமெங்குந் தினவுண் டாகும்
பொருவெடியாய்த் திக்கெனத்தீக் கொழுந்து போல
மெதுமையாய் விட்டெரியும் நல்லபாம்பின்
விஷப்படம் போல் தடித்து வெளுப்புமாகும்
சுதுமையாய்மிகக் சொரியுஞ்சிவப்புமாகும்
தூக்கமொடு சுஞ்சலமும் மிக வுண் டாகும்
கதுமையாய் தோலெல்லாந் தடிப்புண்டாகும்
கனத்த விற்போடகமான குட்டந்தானே".

-யூகி முனி வைத்திய சிந்தாமணி 800, செய்யுள்- 498.

Characterized by elevated skin lesions with erythema and itching. Burning sensation will be present. These entities are associated with anxiety and despair.

சதாரு குட்டம்[7]:

"சித்தானதண்டிப்பாய் ரத்தவர்ணம்
செழும்பச்சை வெள்ளையாய்ச் சிவப்புமாகும்
எத்தான் வெரிப்போடு தினவுமாகும்
எளிதான சேட்டுமவாதத் துற்பத்தி
பத்தான கரடுகட்டிப்புண்ணுமாகும்
பாம்பு தோல் போற்றிரைந்துபருத்துக்காணும்
வெத்தான மூக்கோடு காது கன்னம்
மிகத்துடிப்பாஞ் சதாரு குஷ்டந் தானே".

-யூகி முனி வைத்திய சிந்தாமணி 800, செய்யுள்- 513.

Characterized by skin lesions covered with silvery white scales, erythema, itching, burning sensation and thickening of ears, cheeks and nose

Clinical Features

- The lesions are patches and macules which are red in colour with raised margin and the lesions are covered by silvery, white and rough thick scales.
- The patches are coin shaped over them. In some, the shape may be either round or oval.
- There are variations in the size and shape of patches according to the site.
- The skin lesions occur all over body, commonly front of the knee and back of the elbows affected

- Excessive scaling and generalized erythema develops all over the body.
- In children this lesion may be like water drops and these may occur in scalp and face.
- Mild oozing will be present if flexure region (axilla, groin & infra mammary regions) are involved in females.
- One fourth of patients have nail involvement like pitting and dimpling in nature
- 7% of patients develop affection of joints as psoriatic arthropathy.

3a.1.9.Prevalence of *Kaalanjaga padai*

- 2% of population affected by psoriasis
- 5-25 years is the commonest age group
- Remission and relapses occur
- Females are commonly affected than males

***3a.1.10.Kalanjaga vaatham* (Psoriatic Arthropathy):**

Kalanjagapadai is often associated with painful joints known as "*Kalanjaga vaatham*". It may affect any joint. The most often affected joints are terminal inter-phalangeal joints. In these cases, the affected fingers show nail changes. This combination is termed"Psoriatic arthropathica".

Yugi muni describes the clinical features of *Kaalanjaga vatham* as follows:

"வாதமாங் கால்கையில் குரங்கி ரண்டும்
வருத்து சந்துமுறுக்கியே குடைந்து நொந்து
நாதமா நடைதானுந் தான்கொடாமல்
நலிந்துமே முடமாகிக் கரடு கட்டிச்
சேதமாஞ் சடந்தானு மிகவெ ளுத்துந்
தின வோடு சிரங்குமாய்ச் சேட்ப மாகிக்
காதமாய ருசியொடு மயக்க மாகும்
கருதிய காளாஞ் சகமாம் வாதமாமே".- (செய்யுள்- 259)

The joints of fingers, feet, ankles, knees and sacroiliac are selectively affected and these joints are painful. The deforming erosive arthritis targets fingers and toes. Marked cartilage destruction and bony articulation results in loss of joint space and marked instability. The whole body becomes pale (anaemic). Lesions of well-defined erythematous papules which are sharply demarcated appear on the skin. There is also loss of taste and giddiness.

3a.1.11.Differncial Diagnosis:

Karappan (Eczema):

Kollavae udambellam vedhuppaai nonthu

Kudainthumae migachsurandhu veekkamaagum

Villavae thaegamellaam punpol nonthu

Vediththumae punnagum viralgal santhu

Mullavae mudangiyae narambu thaanum

Mazhikalpakka mikkaida migavu larnthu

Mallavae meniyadhu varandu kaanum

Vaadhamang karappaanran vanmai thaanae**.**

-Yugi muni

- Itching is present in the patches.
- Bleeds / oozes on scratching

Padarthamarai (Tinea infection):

Koodumae thamarayin poovithalpol

Kuvindhidumae karupodu veluppumagum

Thedumae sivappu pala vanna magundh

Thinavumiga vagiyae soriyum senneer

Vadumae iyathinur pathi yagi

Varuthamiga vundaagi novumegum

Podumae sareerangal mugangal kaalgal

Pundareega kuttathin pudhumai thanae.

- Yugi muni

- This is caused by kapha.
- Patches are like lotus petals in the body.
- Patches are black, white, red in colour.
- Itching is present in the patches.
- Bleeds / oozes on scratching.
- The discharge resembles rose water.
- The lesions may be tender and painful.

3a.1.12.PATHOLOGY OF *KALANJAGA PADAI*

The *Kalanjagapadai* affects the skin and mucous membrane.

MUKKUTTRA VERUPADUGAL[7] :

"தாது முறையெ தனிஇடை வாதமாம்
போதுறு பின்கலை புகன்றது பித்தமாம்
மாது சுழிமுனை வழங்கிடும் ஐயமாம்
ஒரு முறை பார்த்து உணர்ந்தவர் சித்தரே"

– பதிணெண் சித்தர் நாடி சாஸ்திரம்.

"மிகினுங் குறையினும் நோய்செய்யும் நூலோர்
வளிமுதலா வெண்ணிய மூன்று"

-Saint Thiruvalluvar

Human body is influenced by three Thathus such as *Vaatham, Pitham* and *Kabam*. They are responsible for normal physiological conditions of the body.The particular thodam increase or decrease (Thannilai piralthal) then it influence the other thodam(vetrunilai valarchi) and cause murkuri or premonitory symptoms in the localized area of the body and later the typical signs and symptoms blows out. In the tertiary stage all the three thodams are vitiated which is called mukkutram stage (sannipatham).This condition becomes incurable. According to the text book ***Siddha Maruthuvam Sirappu*** in *Kalanjagapadai*, the following *Mukkutram* are commonly affected,

உடலின் ஏழு தாதுக்களும் மெலிவடைந்தாலும் மெலிவடையாவிட்டாலும் பித்தப் பொருட்களின் உணவாதி சேர்க்கையால் அதிகரித்து பித்தமானது சமானத்தை அடைந்து, பித்தம்,பித்தவாதம்,பித்தகபம்,முக்குற்றம், இவைகளில் தனித்தனியும் கூட்டுறவுமாகிய சம்பந்தங்களைக் கொண்டு இரத்த,இரச தாதுக்களைக் கொதிக்கச் செய்து, அச்சமான வாயு பிரகோபித்து பித்த கபங்களை ஆங்காங்கு செல்லாது தடுத்து, அதிக சித்த பித்தம் ஆமத்துடன் கூடி அவ்வாமத்தை விரித்திக்கச் செய்தும் சணிக்கச் செய்தும், இரத்த கப,மல,சல, கெடுதிகளைக் கொண்டும் குட்ட ரோகம் உண்டாகின்றது.

- சீவாரட்சாமிர்தம்[7]

Table.3a.1.1.காளாஞ்சகப்படையில் முக்குற்ற குறிகுணங்கள் :

வாதம்	பித்தம்	கபம்
கருப்பு, கருஞ்சிவப்பு	சிவப்பு/மஞ்சள்/பச்சை	வெண்மை
வறட்சி	எரிச்சல்	நீர்த்துவம்
வெடிப்பு	சூடு	பசுமை
பிளப்பு	புண்	தடிப்பு
வலி	கொப்புளம்	சீழ்
சுரசுரப்பு	சிதைவு	அழுகல்
செதில்		கிருமி தாபிதம்
பரவல்		

***Vatham*[8]**

1. Pranan - Occasionally difficulty to breath in BA with KJP patients
2. *Abanan* - Habitual Constipation
3. *Udhanan* - Erythematous changes in the affected areas of skin
4. *Viyanan* - Dryness of the skin in the affected areas of skin
5. *Samanan* - Due to other vaayus, it is affected
6. *Kirukaran* - Loss of appetite
7. *Devathathan* - Laziness, sleep disturbance

***Pitham*[8]**

1.Anarpitham - Loss of appetite& In APD patient ; acidity, burning sensation of epigastric regionin very few cases

*2.*Ranjaga pitham - Erythematous changes in the affected areas of skin,Paleness of the conjunctiva and tongue

3. Sadhaga pitham - Difficulty to do the routine works and sluggishness

*4.*Prasaga pitham - Dryness and roughness of skin

***Kabam*[8]**

1.*Tharpagam* - Burning sensation of eyes may be present

2.*Sandhigam* - Mildjoint pain present in very few cases

Udalthathukkal[8]

The structural components or the tissues components of the body are composed of seven type of materials called *Udal thathukkal or Udal kattukal.* It gives strength and structure to our body. In *Kalanjagapadai patients,* the following *Udal thathukkal* are commonly affected,

Saaram	: Dryness, roughness, tiredness
Senneer	: Erythematous patches present
Kozhuppu	: Synovial fluid secretion affected
Enbu	: Joint pain present in few cases

Natural ability - உடல் வன்மை[8] :

"பருவுடலின் வன்மையே சூக்கும உடலின் வன்மை"

உடல் வன்மை என்பது நம் மனநலனோடு, உடல் வலிவும் இணைந்ததாகும். ஆன்ம உடலின் (மனம்) வளர்சிக்கு ஆதாரமாய் இருப்பது ஸ்தூல உடலின் வன்மைதான்.

"உடம்பினா லன்றி யுணர்வு தானில்லை
உடம்பி னாலுன்னியதே யாம்
உயிர்க்குறுதி யெல்லா முடம்பின் பயனே
அயர்ப்பின்றி யாதியை நாடு"
- ஔவைக்குறள்

It is classified into 3 types, they are

Iyarkai Vanmai (Genetic)

Natural immunity of the body by birth.

Seyarkai Vanmai (Acquired)

Improving the health by intake of nutritious food materials and medicines.

Kaala Vanmai (Related to age,climate,habitat)

Development of immunity according to age and the environment.

When the *Udal vanmai* is affected there may be possibilities of occurrence of *Kalanjagapadai*.

Iymporigal[8] (Sense organ)

In *Kalanjagapadai,*

Mei : Affected (Roughness of the skin, white silvery scales is seen).

Kanmenthriyam[8] (Motor organ)

In *Kalanjagapadai*,

Kai, Kaal : Affected (Difficulty in using the limbs)

Eruvai : Affected (Constipation is seen)

Kosam - (Sheath)[8] :

In *Kalanjagapadai patients,* the following *Kosam* are commonly affected,

Annamaya Kosam (Physical Sheath) : Affected (loss of appetite and acidity in APD with KJP patients)

Pranamaya Kosam (Respiratory Sheath) : Affected (Difficulty to breath in BA with KJP patients)

Manomaya Kosam (Mental Sheath) : Affected (Stress)

Seasonal variations[1] :

Weather and environment changes that affect the health of the individual in each *Kaalam* due to certain life style modifications. The Siddhars have classified the time scale of a year into 6 *Kaalam* it is known as six *perum pozhuthu.*

Table.3a.1.2. Seasonal variations

Season (Perumpozhuthu)	State of Thodam
Ilavenil kaalam (Early summer season) Chithirai – Vaikasi (Mid April to Mid June)	Kabam aggravated
Mudhuvenil kaalam (Latter summer season) Aani – Aadi (Mid June to Mid August)	Vatham accumulated Kabam mitigated
Kaar kaalam (Early rainy season) Aavani – Purattasi (Mid august to Mid October)	Vatham aggravated Pitham accumulated
Koothir kaalam (*Late rainy season)* *Iypasi – Karthigai* (Mid october to MidDecember)	Pitham aggravated Vatham mitigated
Munpani kaalam (*Early winter season)* *Markazhi -Thai* (Mid December to Mid February)	Pitham mitigated
Pinpani kaalam*(Late winter season)* *Masi -Panguni* (Mid February to Mid April)	Kabam accumulated

Prevalence and the signs and symptoms of *Kaalanjaga padai* will aggravated in above mentioned months due to seasonal changes according to the state of humor by certain life style modifications and maybe affected of kaala vanmai.

3a.1.13.Piniyariyum muraimai (Diagnostic Methods)[8]

"மதித்திடற் கருமை வாய்ந்த
மாண்பரி கார மெல்லாம்
துதித்திட வுணர்ந்தா னேனுந்
துகளறப் பினியின் றன்மை
பதித்திட வுணரா னாகிற்
பயனுறா னாக லானே
விதித்திடு பிணித்தி றத்தை
விளம்புது முதற்கண் மன்னோ"
- சிகிச்சா ரத்ன தீபம்

Diagnostic methods in Siddha medicine are very unique and are solely dependent upon the clinical acumen of the physician.

- *Poriyal aridhal (Understanding by the five organs of perception,nose,tongue,eyes,skin,and the ears)*
- *Pulanal aridhal (Understanding by the sense objects smell, taste, vision, somatic sense and sound)*
- *Vinaathal (Interrogation)*

The physician using his organs of perception and senses examines the patient and diagnosis the disease.Apart from this,an appropriate history taking also helpis one to diagnose properly. However, it should be noted that the interrogation comes only finally after physical examination. The diagnosis method id called “Envagai thervu (Eight tools of diagnosis)”

Envagai Thervugal **(Eight tools of examination)[8] are:**

“நாடிப்பரிசம் நாநிறம் மொழிவிழி
மலம் மூத்திரமிவை மருத்துவராயுதம்”.

“அகத்துறு நோயைக் கரத்தாம லகம்போல்
பகுத்தறிவீர் நாடிப் பரிசம் - தொகுத்தநிறம்
கட்டுவகைச் சொல்மொழிகண் கண்டமல மூத்திரம்நா
எட்டுவகை யாலுமறி வீர்"

-அகத்தியர் மணி 4000

***Naadi* (Pulse):**

"மேலுரைத்த நாடியெங்கு மேவினால் உன்பாக
மூலம் கரமூல மூலமேல் - நூலளவே
திண்டி நின்றால் வாதபித்த சிலேட்டுமமென மூன்றாகும்
தாண்டி நின்றால் ஆச்சரியந்தான்"

- *அகத்தியர் மணி 4000*

Pulse diagnosis is a quick, inexpensive, and non-invasive bedside diagnostic tool. Normally the pulse is recorded in a radial artery in the right hand for the male, in the left hand for the female by keeping the ring finer (*vatham*) ,the middle finger (*pitham*) and the index finger (*kabam*) over the artery after gently scrubbing the area.

In *Kalanjagapadai*, the following types of *Naadi* could be felt.

They were,

a) Pitha vatham

b) *Pitha kabam*

c) Vatha pitham

d) Vaatha kabam

e) Kaba pitham

***Sparism (Skin)*:**

"வெம்மை குறைந்தாலு மிகுந்தாலு வாதபித்தம்
தம்மை நிரைநிரையாய்ச் சாற்றுவார் - வெம்மையன்றி
சீதமுஅவ் வாறாகில் சிலேட்டும மொன்றுதொந்த
மீதமும்அவ் வாறாகு மேல்"

--அகத்தியர் மணி 4000

The physician must have ability to identify tactile sensation. Warmth indicates *Pitham*, chillness *kabam*and dryness *vatham.*

In case of *Kalanjagapadai*, slightly raised well defined dry erythematous macules or plaques, covered with white silvery scales,dryness, Burning sensation can be noticed in affected areas.

***Naa* (Tongue):**

"முள்ளாய் வெடித்துக் கறுத்துதான்முன் பின் வெளுத்துத்
தள்ளாநீ ருண்டோசேர்ந் தால்பசந்தால் - எல்லாம்
நடுவாம் பலபலவாம் நற்சன்னி முன்னோய்
ஓடுநரில் நாவென்றோது"

- *அகத்தியர் மணி 4000*

A whitish tongue indicates *Kabam* imbalance and mucous accumulation. A red or yellow green tongue indicates a *Pitham* imbalance , A *Vatham* imbalance is manifested by a black to brown coloration on the tongue.

In case of *Kalanjagapadai* abnormality of tongue like geographical tongue may be noted.

***Niram* (complexion):**

"உரத்தகறுப் பான்வாத ரோகிபித்த ரோகி
அரைத்தமஞ்ச ளைக்குளித்தோன் ஆவான் - இரத்தம்
குளித்தவனு மாவான் கொடும்சிலேத்தும ரோகி
வெளுத்திடுவான் தொந்தரோகி யே"

--அகத்தியர் மணி 4000

Vatham person's skin black in colour ; *Pitham* person's skin either yellow or red in colour, the person with whitish skin belongs to *Kabam*.The body temperament is predominantly mixed in nature i.e *Vatha kabam,Pitha vatham* etc.The colour of the skin also varies on mixer of thirithodam.

In case of *Kalanjagapadai*, Erythematous, hyperpigmented patches with silvery scales could be noticed at affected areas.

***Mozhi* (Voice):**

பலரோகி வார்த்தைப் பலவிதமாம் வாதத்
தலைரோகி வார்த்தைச் சமமாகும் - நிலைகடந்த
பித்தரோ கிக்குஉயர்ந்த பேச்சுண்டாம் சிலேட்டுமந்தான்
சத்தம்ஈ னரமாம் தான்

- *அகத்தியர் மணி 4000*

The normal speech indicates *Vatham*, a high pitched voice *Pitham*, and low pitched voice like *Kabam*.

In case of *kalanjagapadai* high, low pitched voice and medium pitched voice were observed.

***Vizhi (*Eye):** `

கண்கறுத்து நீரோடில் காலாம் நடுவாகில்
கண்பசக்கும் சொக்கும் கடையாகில் - கண்பீளை
சாடி வெளுக்குமே சன்னிவாதம் பித்தமுமென்
றோடியகா மாலை பசக்கும்

-அகத்தியர் மணி 4000

A muddy conjunctiva indicates *Vatham* , yellowish or red – *Pitham* , pale – *Kabam*.

In case of *Kalanjagapadai*, no abnormality was seen in *Vizhi.*

***Malam* (Stool)**:

கறுத்தமல பந்தமலங் காலாகும் பித்தம்
சிறுத்தமுட் டிணம்செம்மை சேரும் -பொறுத்தொருக்கால்
சீதமலந் தில்லையுமாம் சேர்ந்தபல ரோகியாம்
மீதமலம் எண்ணிறமு மே.

-அகத்தியர் மணி 4000

Black coloured constipated stools indicated *Vatham*, yellowish or reddish with diminished quantity and more heat indicated *Pitham* and it is whitish in *Kabam*.

In case of *Kalanjagapadai*, constipation was reported in some cases.

***Moothiram* (Urine):**

In Siddha system,urine is a constituent of Pitha.It is a waste product of blood,which is also a pitham constituent.It is the end product of various metabolic activities taking place in our body.Metabolism itself is a normal function of pitham. Urine contains excess water and dissolved waste materials filtered from the blood by the kidney. Normal urine contains excess water, salt, minerals, urea from protein digestion, uric acid, creatinine from muscle breakdown, hormone wastes, dead blood cells and toxins.So urine is an index of blood. Any pathological changes in urine reflects the pathology of blood. Among various parameters of urine analysis such as colour , smell, froth, specific gravity, and quantity / deposits.

"Therayar" one of the pioneer in Siddha pathology, classified the examination of urine into two main categories.

1.Neerkuri

2.Neikuri

"வந்த நீர்க்கரி எடை மணம் நுரை எஞ்சலென்
றைந்தியலுளவை யறைகுது முறையே"

Neerkkuri :

In neerkuri various parameters of urine analysis such as

Niram	- Colour
Edai	- Specific gravity
Manam	- Smell
Nurai	- Froth
Enjal	- Quantity / Deposits can be noted

Colour :

Normal	- Thurinji pazha niram (*Citrus aurantium* fruit)
Yellow ,Red	- Hot food

தேரையரின் நீர்க்குறி நெய்க்குறி நிச்சயத்திற்குரிய நீர் இலக்கணம்

"அருந்துமா றிரதமும் அவிரோ தமதாய்
அஃகல் அலர்தல் அகாலவூண் தவிர்ந்தழற்
குற்றள வருந்தி உறங்கி வைகறை
ஆடிக் கலசத் தாவியே காதுபெய்
தொருகூர்த் தக்கனலக் குட்படு நீரின்
நிறக்குறி நெய்க்குறி நிருமித்தல் கடனே" [8]

நோயுற்றோர்க்கு மேற்படி விதிவிலக்காம்

"அருப்ப முற்றார்க் கவ்விதி விலக்கே" [8]

Prior to the day of urine examination the patient is instructed to take a balanced diet. The patient should have good sleep. After waking up in the morning, the first urine voided is collected in a clear wide mouthed glass container and is subjected to analysis of "*Neerkkuri*" within one and a half an hour.This rule exclude when and emergency period severe condition of disease condition.

In a *Kalanjagapadai* patients, *Citrus aurantium* fruit colour, wild citrus medica fruit colour, Hey soaked rain water colour and Reddish yellow colour was noticed.

Neikkuri

The collected specimen (Urine) is kept open in a glass dish or china clay container. It is to be examined under direct sunlight, without any shaking of the vessel.

Then add one drop of gingelly oil in from 1cm above the urine specimen without disturbing the urinary specimen and the *neikkuri* was noted in direct sunlight and conclude the diagnosis.

Importance of Neikuri :

- ✓ Findout the clearcut kuttram
- ✓ Rule out the curable and incurable of disease
- ✓ Assessment of prognosis

நெய்க்குறியில் முக்குற்ற வேறுபாடுகள் :

Character of *Vaathaneer*

வாதம் : வாயு + ஆகாயம் (இலேசு) அருவம்

"அரவென நீண்டினஃதே வாதம்"

When the oil drop spreads like a snake, it is called "*Vaatha neer*"

- உடனடி பரவல்
- வேகமான பரவல்
- ஒழுங்கற்ற வடிவம்

Character of *Pithaneer*

பித்தம் : தீ - அருவுருவம் - (நடுநிலை)

"ஆழி போற்பரவின் அஃதே பித்தம்"

When the oil drop spreads like a ring, it is called "*Pitha neer"*

- சீரான வேகம்
- உடனடி பரவல்
- வட்டமான பரவல்
- ஒழுங்கான வடிவம்

Character of *Kabaneer*

கபம் : மண் + நீர் - உருவம்- (பளு)

"முத்தொத்து நிற்கின் மொழிவதென் கபமே"

When the oil drop appears like a pearl, it is called "*Kaba neer*"

- நிலைத்தல்
- பரவாமை

Character of *Thonthaneer*

Snake in the ring, ring in the snake, snake in the pearl and ring in the pearl are the characters of *Thontha neer (mixed type).*

தொந்த நிலை :

உதாரணமாக,

1. கபவாதம் : முத்துப்போல் நீண்ட நேரமிருந்து பின்னர் ஒழுங்கற்ற வடிவமாக மாறுதல்

2.பித்தவாதம் : சீரான வளையமாக துவங்கி ஒழுங்கற்ற வடிவமாக மாறுதல்.

சிகிச்சை முன்னேற்றம் அறிதல் :

சிகிச்சை வழங்கி நோயின் தீவிரம் குறையும் பொழுது வேகம் குறைதல்,மெல்லப் பரவல் போன்றவற்றை நோய் தீவிரம் குறைவதை உணர்த்தும்.

தேரையர் தனிச்சிறப்பு :

சல்லடைக் கண் போன்ற நெய்க்குறி உள்ள நோய் தீராதுஎன நிராகரித்துவிடாமல் கபம் என அணுகும் முறை.[8]

In *Kalanjagapadai,* the Neerkuri was manjal, sivappu majal and *Neikkuri w*as ***Vaatha neer, Pitha neer*** *and* ***Kaba neer,Thondha neeer.***

CLINICAL APPLICATION OF MANIKADAI NOOL TECHNIQUE[8] :

Reference ; Agathiyar Soodamani Kayaru Soothram

Manikadai nool is one among the tool of examination in siddha system to diagnose the disease as well as to assess its prognosis. This unique method was revealed by siddhar *Agathiyr* to his disciple *Vedhamamuni*.The literary meaning of the terminology ;

Manikadai Nool = Mani +Kadai + Nool

Mani = The protuberance of wrist; Kadai= The finger breadth; Nool; Thread

"Manikadai naalviral thalli vanmaiyaai

Thanikidai kayaru pottalandhu paarakaiyil

Kanithidum viralthanai kandu solavey

Pinithidum noyigalai pirithuraikumey"

-Agathiyar Soodamani Kayaru Soothiram

The circumference of the forearm of an individual at the region of 4 finger breadth proximal to the radial protuberance of wrist is measured by using a thread, which should be non elastic. Then the length of the thread is converted in terms of finger breadth units (viral kadai) of the concerned individual patient.

PROCEDURE :

- The region of 4 finger breadth proximal to the radial protuberance of wrist is selected.
- Using the thread the circumference of selection is taken
- The length of the thread is converted in terms of finger breadth units (viral kadai)
- Count the total length of thread in terms of finger units (viral kadai)

Figure.3a.1.1.Manikadainool

PRECAUTION :

- Don’t use any elastic type of thread or twines which may lead to false reading
- Avoid too much loose and tight during measuring the circumference of the selected forearm.
- The measurement should be converted into finger breadth units with the finger breadth of concerned individual patient.
- Don’t measure at the affected forearm like individuals suffering with hemiplegia, fracture, deformity etc.

ADVANTAGE OF MANIKADAINOOL :

- Priceless procedure for arriving diagnosis
- Time consumption is very less
- Prognosis also can be confirmed
- Simple and painless procedure
- No need of any specific skill in employing this technique.

எட்டேமுக்கால்

"எட்டினில் முக்கால் காணில் யிலிக்கிய வுடம்பு காயம்,
தொட்டிய குட்டம்போலே சில்விடம் பலவுந் தோன்றும்,
முட்டிய வயிற்றினுள்ளே முளைபோலே வாயு குத்தும்,
வெற்றிய கண்வாய் கைகள் வெழுத்திடும் பித்த ரோகம்".

எட்டரை

"விட்டுடனிருமலும் வெதுப்பு மேலெல்லாம்
கிட்டிடுஞ் சிலையுங் கிரங்கிக் காணுமே"

- அகத்தியர் சூடாமணிகயறு சூத்திரம்

Table.3a.1.3.Manikadainool

Finger breadth	**Pointedout of description of the stanza**
7 ¾	Head ache,Piles,Epistaxis,Kandamaalai.
8	Loss of appetite,Bloating and upset of stomach,Fever
8 ¼	Body ache,Head ache,Sinusitis,TB,Hydrosis
8 ½	Fever, Cough and giddiness, Kudalvatha, Thathunattam, **Skin diseases like kuttam**, Silanthi, Vettai and Sori
8 ¾	Fever, **Skin diseases like kuttam**,Piles,Eye disease,Sinusitis
9	Pain Lumbar and thighs and difficulty in walk,Ear hearing problem
9 ¼	Insomnia,Sinusitis,Buring sensation of eyes, Burning mituration
9 ½	Fever, Loss of appetite, Buring sensation of eyes,Swlling of whole body
9 ¾	Cough,Dryness,Fissure,Araiyaappu
10	Pain in all over the body,Gastritis,Peptic ulcer
11	Inflated of the body,only death is destiny.

In case of Kalanjagapadai patient'smostly viral kadai was 8 ¾ , 8 ½ finger breadth and complaints of the patient was correlated with the description of the stanza, pointed out for 8 ¾ , 8 ½ finger breadth.

3a.2.LINE OF TREATMENT

The treatment in Siddha medicine is aimed at maintaining the three dhoshams (life constituents) and seven thathus (physical constituents) in equilibrium.Proper diet and regimen of life including cleansing therapies are advised for a healthy living and to restore equilibrium of dhoshams in the early stage of the disease.

"நோய்நாடி நோய்முத னாடி யதுதணிக்கும்
வாய்நாடி வாய்ப்பச் செயல்".

-திருவள்ளுவர்

Thiruvalluvar says in **"Thirukkural"** about physician's duty to study the disease, study the cause, seek subsiding ways and do what is proper and effective.

"உற்றவன் தீர்ப்பான் மருந்துழைச் செல்வானென்
றப்பனாற் கூற்றே மருந்து".

-திருவள்ளுவர்

In *Siddha* system of medicine, the main aim of the treatment is to cure *Udalpini* and *Manapini.* Treatment is not only for perfect healing but also for prevention and rejuvenation. Line of treatment is as follows**:**

- *Neekam* (Treatment)
- *Niraivu* (Restoration)
- *Kaappu* (Prevention)

***3a.2.1.Neekam* (Treatment)**[1]

- விரேசனம்
- உள்மருந்து
- வெளிமருந்து
- பத்தியம்

***Virechanam*:**

"விரேசனத்தால் வாதம் தாழும்
வமனத்தால் பித்தம் தாழும்
நசிய அஞ்சனத்தால் கபம் தாழும்".
"அறிந்திடும் வாதம் அடங்கும் மலத்தினில்".[9]

Detoxification is the first line of treatment used to restore the deranged dhoshams.

First day :

Agathiyar kulambu with 200mg with 30ml leaf juice of Sangankuppi (*Azima tetracantha*) quantity was administered at early morning as purgative (*Kazhichal* Medicine) before starting the treatment for restore equilibrium of dhoshams.

Second day :

Oil bath with *Arakku thylam* has taken at early morning.

Third day onwards from Sunday,Tuesday,Thursday for 48 days :

மருந்துண்ணும் காலம்[8]

“காரி புதம் திங்கள் கருத மருந்தாகாது
பாரினில் சுங்கன் பரிகாரம்- நேரன்று
தேரகுரு சேயுந்தான் தீதில்லை என்றும்
பேரருக்கன் நன்றெனவே பேசு"

- கண்ணுசாமியம்

மருந்தூட்டீங்காலம்[1]

"அனிலநோ யர்க்கசன மாகாமுன் பித்தத்
துனியர்க் கசனநடுத் தூயை- யெனுநோயர்க்
காகாரப் பின்னு மருத்திலுறை யப்பிணியாற்
சாகாரப் பின்னுலகிற் றான்"

"வாதமலாது மேனி கெடாது " [8]

Internal Medicine: *Parangipattai Kudineer*, three times a day before food.

External Medicine: *Sivappu thylam*

***Pathiyam* (Dietary Regimen):**

In mild conditions of the disease, salt and tamarind can be taken in little quantities. When the condition is severe, tamarind should be avoided and salt must be consumed after frying.

“பத்தியத்தினானே பலனுண்டாகும் மருந்து
பத்தியங்கள் போனால்பலன் போகும் பத்தியத்தில்
பத்தியமே வெற்றி தரும் பண்டிதர்க்கு ஆதலினால்
பத்தியமே உத்தியென்றுபால்”

- தேரையர் வெண்பா

“பெருகுஞ் சோள மிறுங்கும் பெரும்கம்பு

வரகு காருடன் வாழையின் காயொடு

உரைகொள் பாகற் கெளிற்றுமீன் உண்டிடில்

விரிவ தாய்க்கரப் பானுமிகுந்ததே”

- பதார்த்த குண சிந்தாமணி

“புளிதுவர் விஞ்சு கறியார் புரிக்கும் வாதம்”

- பதார்த்த குண சிந்தாமணி

Diet Restriction (*Pathiyam*)[57]

- Fish, crab, prawn are some sea foods should be avoided.
- Curd, Jaggery, oil, White gram should be avoided.
- Non vegetarian diet should be avoided.
- Alcohol beverages should be avoided.
- Brinjal should be avoided.
- In severe cases tamarind should be avoided.
- Dietary taken salt in minimum quantities.

3a.2.2.NIRAIVU (RESTORATION)[1]:

Substances used for neutralizing the three humors are**:**

"ஒன்றிய வாத பித்த கபமிவையுயரா வண்ணம்

நன்றுறு கறிகளெல்லாம் நாளுமே சமைப்பராய்ந்த் தோர்

தின்றிடு மிளகு மஞ்சள் சீரக முயர்ந்த காயம்

வென்றி கொள் சுக் கோடேலம் வெந்தியம் உள்ளி சேர்த்தே"

-பதார்த்த குண சிந்தாமணி

The patients are well motivated. The nature and course of the disease is explained to them, Life-style modification advised.

Substances advised for *Vaatha* disease are**:**

“செங்கமுநீர் கோடைத் தேன்மிளகு நல்லெண்ணெய்

தங்கு பெருங்காயத் தமுதாழை - எங்கெங்கும்

கட்டு சிறு முத்து நெய் கோதில் உளுந்திவைகள்

வாட்டு மனிலத்தை மதி.”

-பதார்த்த குண சிந்தாமணி

Honey collected during summer, pepper, gingely oil, asafoetida, castor oil and black gram are very useful in *Vatha* disease.

3a.2.3.KAAPPU (Prevention)[1]

As per siddha system the aetiology of the diseases are various. The ultimate speciality of siddha system is to prevent the diseases.

In the siddha classical text *Pathartha guna chinthamani* has given so many ideal measures to prevent the diseases. These are given below

"திண்ண மிரண்டுள்ளே சிக்க வடக்காமற்
பெண்ணின்பா லொன்றைப் பெருக்காமல் உண்ணுங்கால்
நீர்சுருக்கி மோர்பெருக்கி நெய்யுருக்கி யுண்பவர்தம்
பேருரைக்கிற் போமே பிணி"
"ஆறு திங்கட் கொருதடவை வமனமருந் தயில்வோம்
அடர்நான்கு மதிக்கொருகாற் பேதியுறை நுகர்வோம்
தேறுமதி யொன்றரைக்கோர் தரநசியம் பெறுவோம்
திங்களரைக் கிரண்டுதரஞ் சவரவிருப் புறுவோம்
வீறுசதுர் நாட்கொருகால் நெய்முழுக்கைத் தவிரோம்
விழிகளுக்கஞ் சனமுன்று நாட்கொருகா லிடுவோம்
நாறுகந்தம் புட்பமிவை நடுநிசியின் முகரோம்
நமனார்க்கிங் கேதுகவை நாமிருக்கு மிடத்தே".[1]

The *Siddhar Theraiyar* explains above lines are the rules to maintain healthy life and prevent diseases.

Karpa Marundhukal (Rejuvenative Drugs)[3] :

"Kaya" means body and ***"Karpam"*** means **"strong as stone"**

"Kayakarpam" or "Kayakalpam" is one of the unique special therapeutic divisions in siddha system of medicine advocated specially for rejuvenation, decreasing morbidity and increasing the life span. Thus this discipline details the methods and drugs used for longevity and enhancement of innate health. "Kayakarpam aims strongly on both physical and mental wellness of human being"**.**

"அஞ்சுகத்தி லழியாமற் காயந்தான்
மிஞ்சிய கற்பம் விளம்பினோம் நூற்றெட்டுத்
தஞ்ச முறவே தான் தின்ன வல்லோர்க்குப்
பஞ்சு நரை போய் பதிதோங்கி வாழ்வாரே"

-திருமூலர் வைத்திய பகுதி பாடல்:67

In kalanjagapadai patients ; advised after clearance of kalanjagapadai's symptoms to follow-up the karpamarundhugal,

- ✶ Amukkaraa root (*Withania somnifera*)
- ✶ Seenthil (*Tinospora cordifolia*)
- ✶ Thetran kottai (*Strychnos potatorum*)
- ✶ Ayajambira karpam (iron compound with lime juice)
- ✶ Keezhanelli (*Phyllanthus amaranthus)*

3a.2.4.KARPA YOGAM[3] :

The famous verses from ***Agathiyar Gnanam,*** a Siddha literature speaks about treating the mind as follows;

"*If the mind is good then no need of chanting*
If the mind is good then no need of breathing exercise
If the mind is good then no need of retention of inspired air
If the mind is good then body is good" [3]

A Life free of ailments especially from life style disorders, a proper co-ordination over the psychic stage, psychosomatic stage and organic stage towards the available holistic health and Positive thinking are attained by Yogic practices. The integrated approach of Yoga therapy (IAYT) is the need of the hour in maintaining sound physical, mental and social well being of people globally.

Globalization technological advancement intermixing of work culture, environment changes, recessions and subsequent changes in the nature of work are in fast pace. Stress is associated with everyone at workplace whether rich or poor, young or old, male or female and no none is immune from it. Stress may be the biggest single cause for affect the mind in kalanjagapadai patients. So regular practice yoga may help to manage of stress.

Yoga is a subject of science of higher order, which carries in it the mystery of conservation of health and transformation of life of complete expression of life is possible

through Yoga. The concept of Ashtanga Yogam mentioned in *Thirumandhiram*, a Tamil Siddha literature, have enormous contribution towards holistic health by practising Eight steps of Yoga are outlined here.

- Iyamam (Purity of Mind)
- Niyamam (Purity of Action)
- Asanam (Posture)
- Pranayamam (Breathing technique)
- Prathyaharam (Controlling Sense)
- Dharnai (Concentration)
- Dhyanam (Meditation)
- Samadhi (Contemplation)

Skin is the reflex of mind and so we should treat not only the physical but also treat mind and soul. There by patients are advised to do *yogam* practice.

Asanas like,

- Surya namaskaram (Sun salutation)
- Padmasanam (Lotus position)
- Nadi suddhi pranayamam (Alternate nostril breathing practice)
- Paschimottanasanam (Forward bend pose)
- Makarasanam (Crocodile pose) will be given for IPD patients and these are all beneficial to relieve stress and strain.

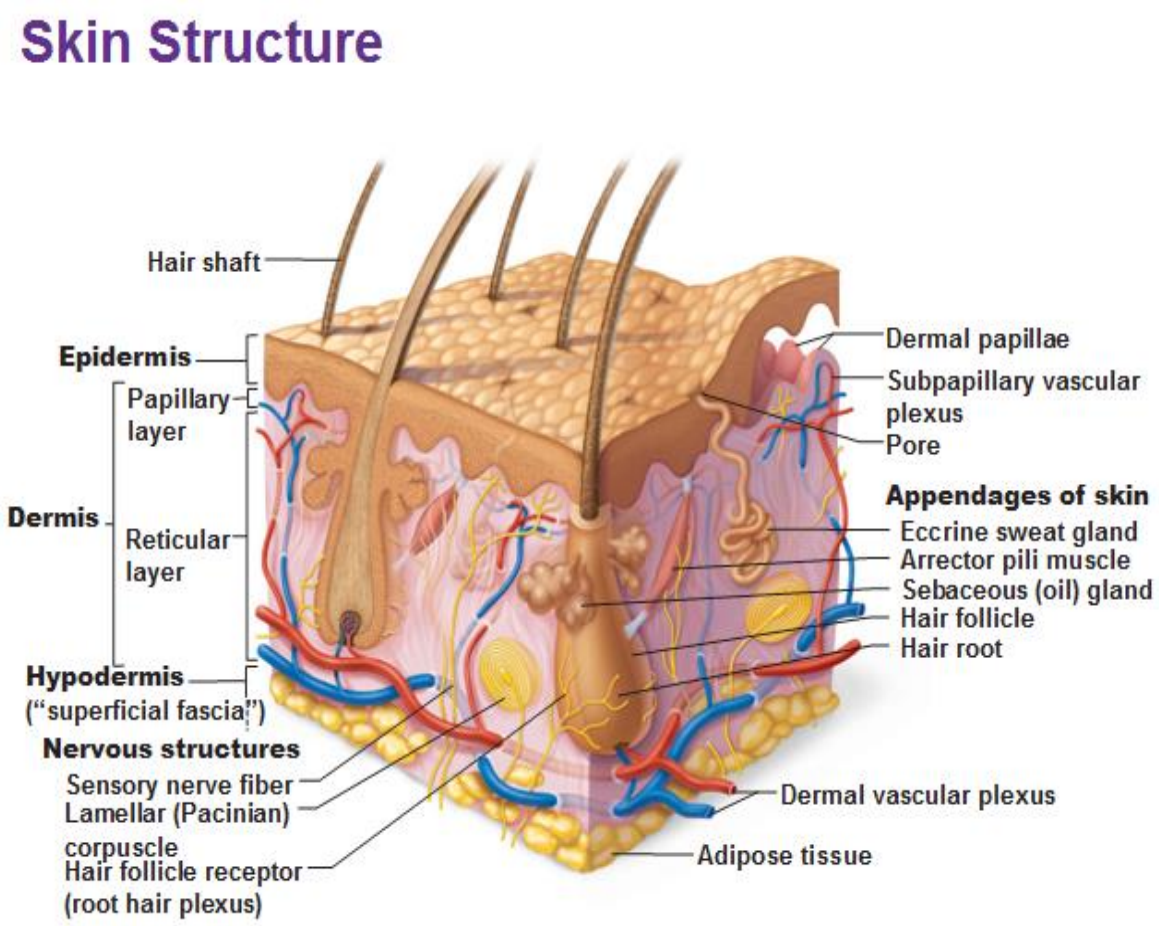
3.b.MODERN ASPECT

3b.1.ANATOMY AND PHYSIOLOGY OF SKIN [9]:

3b.1.1.Anatomy of skin:

The skin or integument is a protective covering of the body. The skin is the largest organ of the body with a total area of about 20 square feet. It is the dividing line between the individual and his external environment.

3b.1.2.Structure of skin:



3b.1.1.Figure Structure of skin

The skin varies in thickness from less than 0.5mm to 3 or even 4mm. It consists of 2 main parts- epidermis of ectodermal origin and an underlying dermis derived from the mesoderm. Below the dermis is the subcutaneous layer of connective tissue.

Structure of epidermis:

Epidermis is formed of stratified squamous epithelium and is non-vascular. Thickness is between 0.07mm and 0.12mm. In soles and palms, it is very thick which ranges from 0.8mm to 1.4mm. The downward projections of epidermis are referred as rete ridges. The colour of the skin is mainly due to melanin, a pigment produced by special cells called melanocytes present in the epidermis.

There are five chief layers of epidermis. They are

1. Stratum corneum
2. Stratum lucidum
3. Stratum granulosum
4. Stratum spinosum
5. Stratum germinativum

Stratum corneum:

This be the most superficial layer. This layer is exposed to the atmosphere. The cells in this layer are non-nucleated and this layer consists of dead cells which are called corneocytes. On application of intermittent mechanical pressure, this layer becomes thicker. This is thickest on the palms and soles. This layer is very thin on the outer aspect of the lips and glans penis and the eyes.The cytoplasm is flattened with fibrous protein known as keratin.Apart from this, these ceels also contain phopholipids and glycogen.

Stratum lucidum:

This layer lies superficial to stratum granulosum.It is made up of flattened epithelial cells.As these cells exhibit shiny character.It is present only palm and sole.

Stratum granulosum:

It is a thin layer with 2-5 rows of flattened rhomboid cells. This cells have keratohyaline basophilic granules. Above the stratum malpighii and near the granular cell layer, odland bodies are seen. The odland bodies take part in the barrier function of the epidermal permeability.

Stratum spinosum (Stratum malpighi) :

It is also known as prickle cell layer because the cells of this layer possess some spine like protoplasmic projections.By this projections, the cells are connected to each other by intercellular bridges.

Stratum germinativum:

The deepest portion of the epidermis is stratum germinativum. It is made up of polygonal cells superficially and columnar cells in deeper parts. Since the entire dermis is germinated from this layer, it is named as stratum germinativum. Trauma to this layer leads to scar formation. Melanoblasts, melanocytes and Langerhans cells are present in this layer.

Dentritic cells of epidermis (special epithelial cells):

The epidermis contains 3 types of specialized cells. They are

a. The melanocytes
b. The langerhans' cells
c. The Merker's cell or touch cell.

Epidermal appendages :

Sebaceous gland,sweat gland,hair, and nails are the epidermal appendages.

Structure of dermis (cutis vera or corium) :

The dermis is the inner layer of the skin which is rich in blood vessels, lymphatics and nerves. and it is composed of collagen fibers,fibroblasts,histeocytes. The collagen fibers exhibit elastic property and are capble of holding water.The collagen fiber contain the enzyme collagenase,which is responsible foe wound healing.

Dermis has abundant collagen rich in fibroblasts. Collagen is a protein. It constitutes about 70% of dry weight of dermis. The thickness of dermis is 1- 3mm. Sensory end organs like Pacinian and Meissner's corpuscles, Ruffini corpuscles, end bulb of Krause are present in dermis.

The dermis consists of two parts -

a. Superficial papillary dermis
b. Reticular dermis

A. The superficial papillary dermis :

Dermal papillae are finger like projections arising from superficial papillary dermis.It is extending from epidermis. This layer containg pigment cells known as chromotophores.

B. Reticular dermis :

It is made up of reticular and elastic fibers.These fibers are found around the hair bulbs,sweat glands, sebaceous glands.This layer contains mast cells,nerve endings,lymphatics,epidermal appendages and fibroblasts.

3b.1.3.Physiology of skin:

The skin performs a multitude of functions. They are

a. Protection
b. Perception
c. Regulation of body temperature
d. Secretory function and excretory function
e. Absorption
f. Formation of vitamin D
g. Storage function
h. Respiratory function
i. Acid base equilibrium
j. Water balance
k. Psychic function

Protection:

The skin provides protection to the underlying parts against injury, infection, UV rays of the sun. Nails are also protective adjunct of the skin.

Perception :

The skin is rich in nerves and various types of specialized sensory end organs. It contains receptors which mediate the sensations of touch, pain, warmth and cold.

Regulation of body temperature:

Skin plays an important role in heat loss. The skin loses heat to the external environment in 3 ways: by conduction, radiation and evaporation. About 90% of the total heat concentration of the body is regulated by the skin. The sensory end organs of heat (organs of Ruffini) and cold (end bulbs of Krause) also help in regulation of body temperature.

Secretory function:

The important glands present in skin are sweat glands and sebaceous glands. They secrete sweat and sebum. Water, salt, lactic acid and product of nitrogen metabolism, drugs like mercury, arsenic, and iodine etc.are excreted through skin. Sebum is composed of fatty acids, cholesterol, alcohols etc. Fatty acids have a mild fungistatic activity. Sebum and sweat fight against bacteria through certain fatty acids and enzymes.

Absorption:

Intact skin absorbs substances dissolved in fatty solvents similar to vitamins and hormones. Watery solutions are not absorbed.

Respiratory function:

A small amount of gaseous exchange occurs through skin. Small amount of CO_2 is eliminated along with sweat. Nitrogen and oxygen are reabsorbed.

Acid base equilibrium:

A fair amount of acid is excreted through sweat. Thus, it maintains acid base equilibrium.

Psychic function:

Emotional status of a person is expressed through skin. For example ; fear causes blanching of skin and cold sweats.

3b.2.PSORIASIS

The word psoriasis is derived from the Greek word **"PSORA"** meaning **"Itch" or "Rash".** It has been known since ancient times and was originally considered a type of leprosy, It is one of the most common human skin diseases.

3b.2.1.Definition:

Psoriasis is one of the commonest non-infectious, chronic,relapsing,papulo-squamous disorder characterized by erythematous, scaling, plaques of various sizes. The lesions are usually covered by silvery white lamellar scales.[10]

Psoriasis affecting approximately 2% of the population.Most scientific research refers to 85-90% of patients affects by Psoriasis vulgaris.

The disease is usually manifested as raised, well-demarcated,erythematous oval plaque with adherent silvary scales.The scales are a result of a hyperproliferative epidermis with premature maturation of keratinocytes and incomplete cornification with retention of nuclei in stratum corneum (Parakeratosis).The mitotic rate of the basal keratinocytes is increased as compared with that in normal skin.As a result,the epidermis is thickened (acanthosis),with elongated rete ridges: in combination with the dermal inflammatory infiltrate,this contributes to the over all thickness of lesions,which can vary between thick and thin plaque psoriasis and has been proposed as adistinctive trait.

The inflammatory infiltrate consist mainly of dendritic cells,macrophages,and T cells in the dermis and neutrophils,with some T cells in epidermis.The redness of the lesion is due to increase number of tortous capillaris that reach the skin surface through a markedly thinned epithelium.[4]

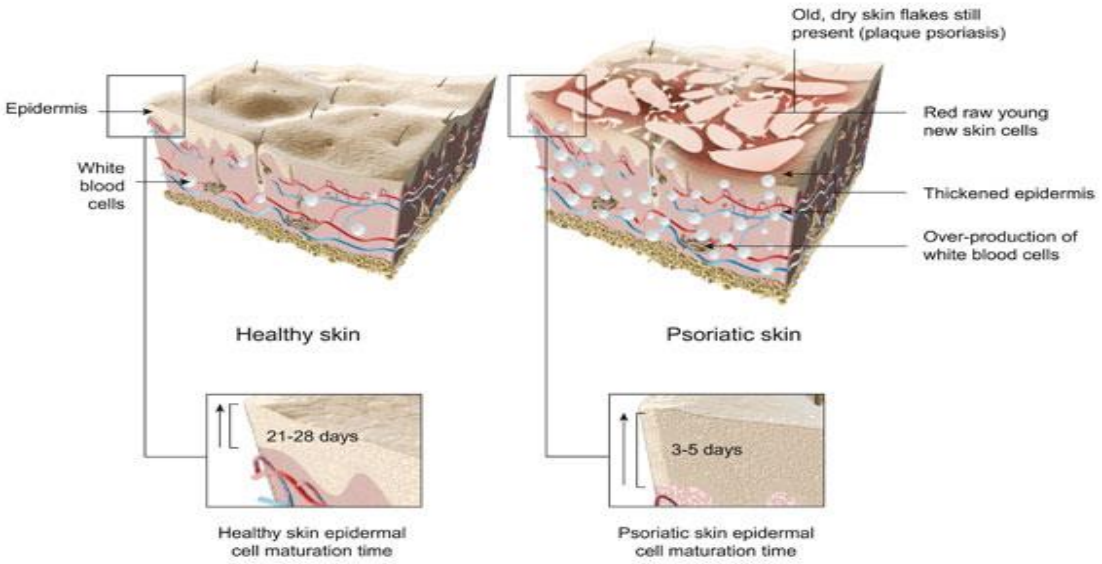


Figure.3b.2.1. Difference between Normal skin and Psoriatic skin

3b.2.2.Etiology[58]:

The etiology of psoriasis isn't fully known, but it's thought to be associated to an immune system.

3b.2.3.Exacerbating Factors:

Factors can be sub divided into, 1) Local 2) Systemic factors.

Local factors:

- Trauma: e.g. Physical electrical, chemical, surgical, skin injury or even too much scratching can worsen or rapid localized psoriasis (Koebner reaction.).
- Sunlight: Most patients commonly consider sunlight to be beneficial for their psoriasis. Most report psoriasis severity is decrease during the summer months or psseriods of increased sun exposure; however, a small minority get that their symptoms are provoked by strong sunlight.

Systemic factors:

- Infection: Pharyngeal streptococcal infections have been shown to make guttate psoriasis. Some proof suggests that subclinical streptococcal colonization (or overgrowth) can be responsible for refractory plaque psoriasis. An increase in psoriasis was noticed in HIV infected patients.

- Drugs: Some of the drugs cause of psoriasis. Lithium and withdrawal from corticosteroids are commonly known to cause flares of disease. Beta-blockers, anti-malarials,tetracyclines. and NSAIDs have also been implicated.
- Psychogenic / emotional factors: Many patients statement an increase in psoriasis severity with mental stress. A clear cause-and-effect relationship between disease exacerbation and stress has not been proven but, itching associated with increased anxiety or depression may promote scratching.
- Smoking: An increased risk factor of chronic plaque psoriasis exists in smokers.
- Alcohol: Alcohol is worsen the severity of psoriasis.
- Endocrine: Psoriasis severity has been noted to fluctuate with hormonal changes. Disease incidence peak at puberty and for the period of menopause. Pregnant patients' symptoms are more likely to improve than worsen. In difference, the disease is more likely to flare in the postpartum period.

3b.2.4.Triggering factors for psoriasis:

Weather

Infections

Injury to the skin

Stress

Smoking,

3b.2.5.PATHOGENISIS [11]:

Role of genetic factors :

There is considerable evidence that genetic factors play a key role in the development of psoriasis. If only one parent has psoriasis, then the risk for the child developing psoriasis is 16%. It increases to a 50% chance if both parents have psoriasis. Twin pair analysis has revealed 72% concordance among monozygotic twins compared to 22% concordance among dizygotic twins. Due to genomic imprinting, men are more likely than women to transmit psoriasis to the offspring. Psoriasis has been associated with many (human leukocyte antigen) HLA haplotypes. By using linkage analysis and genome-wide association studies, at least nine candidate loci have been identified: 6p (PSORS1), 17q25 (PSORS2), 4q34 (PSORS3), 1q21 (PSORS4), 3q21 (PSORS5), 19p13 (PSORS6), 1p32 (PSORS7), 16q (PSORS8) and 4q31 (PSORS9). A few non-major histocompatibility complex (MHC) susceptibility loci have also been identified, but they may be of limited value in disease prediction as they confer a low risk towards disease development. Recently, Chen *et al*. developed a psoriasis global genetic risk

score (GRS) using ten single nucleotide polymorphism (SNP) previously confirmed psoriasis susceptibility loci and observed that of the 10 SNPs evaluated, the strongest signal was found at the *HLA-C* locus at rs10484554, with a 206% elevated risk of psoriasis. They did not find any association between weighted GRS (wGRS; which weights each risk allele by the logarithm odds ratio) and psoriatic arthritis and a marginally significant association between wGRS and guttate psoriasis. In a study from western India, Umapathy *et al*. showed a strong association of HLA-A2, B8, and B17 antigens with psoriasis.

Many authors classify psoriasis as a genetically complex disease as it shares features like the pattern of inheritance, environmental influence and immune dysregulation with diseases such as diabetes mellitus and Crohn's disease. One school of thought is that psoriasis results from the interplay of multiple genes. The drawback of this hypothesis is that although the psoriasis susceptibility genes are located in numerous loci throughout the genome, these locations vary among different populations and families, and the results are difficult to replicate. Goilhou *et al*. hypothesize that the same genes may be present at these different loci as "jumping genes or retrotransposons". This implies that a sequence may be present as multiple copies in the human genome and the disease manifests when one or several copies are activated. Human endogenous retroviruses (HERVs) may fit this criterion. HERVs are the sequences in genome that were probably derived from the viruses many million years ago which then integrated into the human genome and became its integral component during the evolutionary process. These highly repetitive and moderately repetitive sequences are transmitted as Mendelian genes and through retrotransposition.

Moreover, since these HERVs can be activated spontaneously during meiosis or by environmental factors like UV radiation, they may account for the phenomenon of genomic imprinting.

PSORS1 is present in the HLA Class I region of chromosome 6p and accounts for 35-50% of heritability of the disease. HLA-C-*06 is the most likely susceptibility gene in the PSORS1 region and given its important role in antigenic presentation, the association reflects the role of the adaptive immune response in psoriasis. The locus also harbours the corneodesmosin (CDSN) gene, which encodes a protein expressed in differentiated keratinocytes and is considered a genetic risk factor for psoriasis development. Since PSORS1 harbours both the CDSN gene and HLA-C-*06, it is quite possible that both adaptive immunity and defective barrier function are involved in the pathogenesis of psoriasis. enumerates the various genetic loci that have been implicated in the pathogenesis of psoriasis.

Gene/Locus	Function
Genes associated with adaptive immunity	
HLA C or MHC gene	Present antigens to naïve T cells
IL-23R or IL-23 receptor subunit	Maturation of T cells
IL-12B	Maturation of T cells
ERAP1 (Endoplasmic reticulum aminopeptidase 1)	Trimming of peptide antigens for binding to MHC1
TNF-α	Important pro inflammatory cytokine involved in psoriasis
IL-23A/STAT2 or IL-23, subunit p19	Regulation of T-cell activation
IL-23A, α-subunit p19	Regulation of T-cell activation
Genes associated with innate immunity	
IFIH1 (Interferon induced helicase C domain), MDA5	Rig like helicases, involved in recognition of RNA viruses
TNFAIP3 (Tumour necrosis factor-α induced protein 3)/ A20	TNF-α inducible zinc-finger protein that temporarily limits immune response by inhibiting NF-κB signalling
FBXL19 (F-box and leucine rich repeat protein 19)	Inhibition of demethylase activity to activate NF-κB
Genes associated with skin barrier function	
LCE3B and *LCE3C*	Barrier of skin function
CDSN	Component of cornified envelope
DEFB cluster or β-defensins	Antimicrobial and chemotactic function
GJB2 (Gap junction protein β2), connexin26	Involved in gap junction formation

HLA: human leukocyte antigen, MHC: major histocompatibility complex , STAT: signal transduction and transcription, MDA: melanoma differentiation-associated protein, RNA: ribonucleic acid, DEFB: defensin β:, NF: Nuclear factor, LCE3B: Late cornified envelope proteins 3B, TNF-α: Tumour necrosis factor-α, CDSN: Corneodesmosin

Figure.3b.2.2. Genes involved in susceptibility to psoriasis.

Significant associations have also been found in gene regions involving specific inflammatory pathways, namely, IL-23 signaling (IL-23A, IL-12B and IL-23R), modulation of Th2 immune responses (IL-4 and IL-13), and nuclear factor (NF) κB signaling. Other associations include epidermal defense genes, DEFB4 (copy number variation [CNV] of a genomic segment on chromosome 8p23.1 harboring a cluster of DEFB genes, encoding β-defensins), and late cornified envelope proteins 3B (*LCE3B*) and 3C (*LCE3C*) (a CNV in the PSORS4 region on chromosome 1q21 encoding their deletion). These genes are expressed in epithelial cells but not on immunocytes. Epistatic interactions involving HLA-C-*06, endoplasmic reticulum aminopeptidase 1 (which encodes a protease that has an important role

in MHC class 1 peptide processing) and *LCE3C-LCE3B-del* have also been documented. Marrakchi *et al*. observed that homozygous missense mutation in the IL36RN gene on chromosome 2q13-q14.1, encoding for IL-36 receptor antagonist was associated with an unregulated secretion of inflammatory cytokines and an increased predisposition to develop generalized pustular psoriasis.

The role of the NLR/CATERPILLAR (nucleotide binding domain) family of genes in psoriasis has also been studied. These encode important mediators of innate immunity and are concerned with maintaining epidermal barrier function and initiating pathogenic responses to environmental microbes. NLR genes have also been implicated in the causation of Crohn's disease, Blau's syndrome, early onset sarcoidosis, familial cold urticaria, Muckle-Wells syndrome and chronic infantile neurologic cutaneous syndrome. NLR products can be divided into those with N-terminal coiled-coil structures and those with N-terminal Toll like receptors (TLR)/IL-1 receptor domains. NLR gene products like Nod 1, Nod 2 and Ipaf proteins are involved in intracellular recognition of bacterial components and regulation of chemokine secretion and defensin release.

Role of Adaptive and Innate immunity :

Activated T cells are believed to be the primary modulators in the pathogenesis of psoriasis. Disordered cellular immunity involving inflammatory cytokines (IL-1, IL-6, Tumour necrosis factor-α [TNF-α]) and proinflammatory transcription factor (NF-κB, signal transduction and transcription and AP-1) has also been implicated.

Naïve T-cells can differentiate into any of the four types of inflammatory cells (viz. Th1, Th2, Th17 or T regulatory cells) depending on the presence of TNF-α, TGF-β and IL-6. In the presence of TGF-β and IL-6, naive T-cells transform into Th17 cells. These activated cells enter the circulation and extravasate through the endothelium to the sites of inflammation in skin where they produce the Th1-Th2-Th17 imbalance. The role of the IL-23/Th17 pathway has been intensely researched in recent years. IL-23, a heterodimer composed of p19 and p40 subunits, is produced by dendritic cells and macrophages. It causes activation of Th17 cells to produce IL-17 and IL-22. Psoriatic skin lesions contain high mRNA IL-23 levels compared to normal skin. Th17 cells are CD4+ effector cells distinct from the classic Th1 and Th2 lineages and are responsible for providing both innate and adaptive immunity against pathogens. IL-17 (also known as IL-17A) is part of a group of cytokines, called the IL-17 family, consisting of six ligands (A to F), and with five receptor family members. IL-17 cytokines are probaby critical for the pathogenesis of psoriasis. IL-17A and IL-17F are the predominant cytokines released by

Th17 cells, but are also produced by γδ T cells, whereas IL-17C is produced by keratinocytes. The effect of IL-17 cytokines is mediated via the adaptor protein connection to IκB kinase and stress-activated protein kinases (CIKS)/Act1. This is confirmed by the association of psoriasis with the gene encoding CIKS. IL-17A and IL-17F act on keratinocytes to stimulate the production of β-defensins and antimicrobial peptides (AMPs), and chemokines such as IL-8, CCL20 and CCL2. In addition, the IL-17 system may also play a role in antimicrobial defense via maintenance of mucocutaneous immunity. Elevated levels of IL-17 result in an increase in levels of pro-inflammatory cytokines like S-100, A7, β-defensins and lipocalin. In addition, increased levels of β-defensins are associated with relative resistance to infections. Increased levels of IL-17 also promote keratinocytes to produce CXC-chemokines and CCL-20, both of which attract neutrophils to the site of inflammation. Increased IL-22 levels lead to epidermal acanthosis and abnormal keratinocyte differentiation. Ustekinumab, a monoclonal antibody that inhibits the p40 subunit of IL-17, is effective in the treatment of psoriasis. Similarly, Apilimod, an orally administered compound that selectively suppresses synthesis of IL-12 and IL-23, leads to substantial improvement in psoriasis. Analogous to psoriasis, the role of Th17/IL-23 pathway has been investigated in psoriatic arthritis. However, a definite involvement of Th17 cells and related cytokines in human arthritic disease remains to be conclusively proven. Although initial studies with IL-17 antagonists and IL-23 monoclonal antibodies have shown a favourable response in psoriatic arthritis, these results need to be compared with TNF-α inhibitors.

Apart from Th-17 cells, the role of a new subtype of cells, Th-22 cells, is also considered important in the pathogenesis of psoriasis. These cells, on activation by TNF-α, IL-6 and CCL20, exclusively produce IL-22 and are involved in epidermal immunity and remodeling. They express CCR10, CCR6 and CCR4 receptors on their surface. Different dendritic cell subsets might also regulate the Th17 versus Th22 activation with CD11C+ dermal DC's promoting Th17 cells while epidermal Langerhans cells stimulate the Th22 cells.

Finally, angiogenic factors produced by epidermal keratinocytes are now recognized as drivers of abnormal dermal vascular proliferation and angiogenesis.Levels of vascular endothelial growth factor are raised in psoriatic plaque.

The role of innate immune T cells and effector cells like γδ T cells and natural killer cells has also been investigated. Cai *et al*. identified a new subset of γδ T cells in the dermis which, unlike epidermal γδ T cells and conventional αβ T cells, express IL-23R, CCR6 and transcriptional factor RORγt, and release IL-17. These act as the first line of defense against

foreign pathogens and on activation, release mediators that promote and maintain inflammation. Dermal γδ T cells are elevated in psoriasis plaques and may be important in the pathogenesis of psoriasis due to their role in amplifying the adaptive immunity. Mabucchi *et al*. showed that IL-23 failed to induce inflammation in T cell receptor (TCR) δ-deficient mice. Laggner *et al*. found another novel Vγ9Vδ2 T cell subset, which expressed cutaneous lymphocyte associated antigen, to be increased in psoriatic lesions but decreased in the peripheral blood. Functional defects in regulatory T cells (T_{reg}) have been found in psoriasis. This may partly be due to the high levels of IL-6 in psoriatic lesions, which suppress T_{reg} activity and which in turn results in unopposed activity of pathogenic T cells.

Role of impaired skin barrier in psoriasis :

The hallmarks of psoriasis are hyperproliferation and abnormal differentiation of epidermal keratinocytes, infiltration of T lymphocytes, and various endothelial vascular changes in the dermal layer, such as angiogenesis, dilatation, and high endothelial venule (HEV) formation. The skin acts as a two-way barrier to prevent the inward or outward passage of water and electrolytes. The barrier is largely situated in the epidermis, isolated epidermis being as impermeable as whole skin, whereas once the epidermis is removed the residual dermis is almost completely permeable. The epidermal barrier is localized to the stratum corneum. The barrier depends on both the cornified material of the keratinocytes and the intercellular material, particularly lipids. A two-compartment model of the stratum corneum as a barrier is currently accepted, in which protein-rich cells, the corneocytes, are embedded within a continuous lipid-rich matrix. An intact stratum corneum prevents invasion of the skin by normal skin flora or pathogenic microorganisms.

Minor injury in the skin and skin diseases can provide portals of entry to microorganisms, particularly *Streptococci* or Staphylococci. AMPs, peptides present on the epidermis and its appendages, act as the first line of immune defence. The two major groups of AMPs, defensins and cathelicidins, provide a chemical barrier to infection where a physical barrier is absent or limited.

Psoriasis is associated with epidermal defensin genes. Out of 7 β-defensin genes, 6 genes (except *DEFB1* gene) are located on chromosome 8p23.1 over a large repeat unit that can vary in copy number. Case control studies have shown a significant association between psoriasis and increased CNV of the β-defensin gene cluster. Psoriatic lesions are characterized by increased levels of hBD-2 β-defensin. While high defensin levels may account for the lower incidence of skin infections in psoriatic plaques, they also possess potent proinflammatory

activity. They may account for the KP as high β-defensin copy numbers increase the intensity of inflammatory response to minor stimuli. Similarly, cathelicidin LL-37 is overexpressed in inflamed skin in psoriasis, binds to extracellular self-DNA released from dying cells, and converts self-DNA into a potent stimulus for plasmacytoid dendritic cells (pDCs). Subsequently, pDCs secrete type I interferons and trigger an auto-inflammatory cascade.

The abnormal keratinization in psoriasis is seen as an increased expression of early differentiation markers such as CDSN and small proline rich proteins, cystatin A and transglutaminase 1, and decreased expression of late differentiation markers such as loricrin and filaggrin. This leads to aberrant formation of the cornified envelope that in turn affects the barrier capacity of the skin. This manifests as increased transepidermal water loss, which is directly proportional to the clinical severity. The expression of aquaporins, a family of water transporting proteins present in the plasma membrane of the stratum corneum and the stratum spinosum, is decreased in lesional and perilesional skin in psoriasis. The LCE gene cluster, which is composed of six groups (LCE 1-6, with a total of 18 members) is a part of the epidermal differentiation complex. Its deletion has been strongly linked with psoriasis.Deletions of *LCE3B* and *LCE3C* genes are present in 60-70% of the general population. The exact function of *LCE3B* and *LCE3C* genes is not known, but they are induced after minor skin trauma such as tape stripping. de Cid *et al*. found significantly increased expression of LCE3 genes and reduced expression of other LCE genes in psoriastic plaques. de Guzman Strong *et al*. found that loss of the 32.4 kb region which functions as an epidermal specific enhancer and is present adjacent to the *LCE3B* and *LCE3C* genes, may be the initiating event in psoriasis. It has been speculated that deletions of *LCE3B* and *LCE3C* genes lead to incomplete barrier repair after minor trauma, which in turn causes penetration of various antigens and induces an inflammatory response.

Interaction of damage associated molecular patterns (DAMP) and the pathogen associated molecular patterns (PAMP) with their receptors, such as TLR and NOD like receptors, causes the activation of keratinocytes and the epidermal innate immune system and thus, increased secretion of antimicrobial proteins. This interaction between DAMP/PAMP with TLR/NOD like receptors is also followed by liberation of inflammatory cytokines such as TNF-α, IL-8 and IL-1β, all of which are potent chemoattractants. In patients who carry the psoriasis susceptibility genes, such as HLA-C*06, LCE3B/LCE3C-del or defensin genes, exposure to PAMP leads to a heightened inflammatory response and defective skin barrier repair with

increased expression of keratins 6 and 17, and the LCE3 family. Aberrant skin repair allows a sustained exposure to PAMPs which are engulfed by Langerhan cells and dendritic cells.

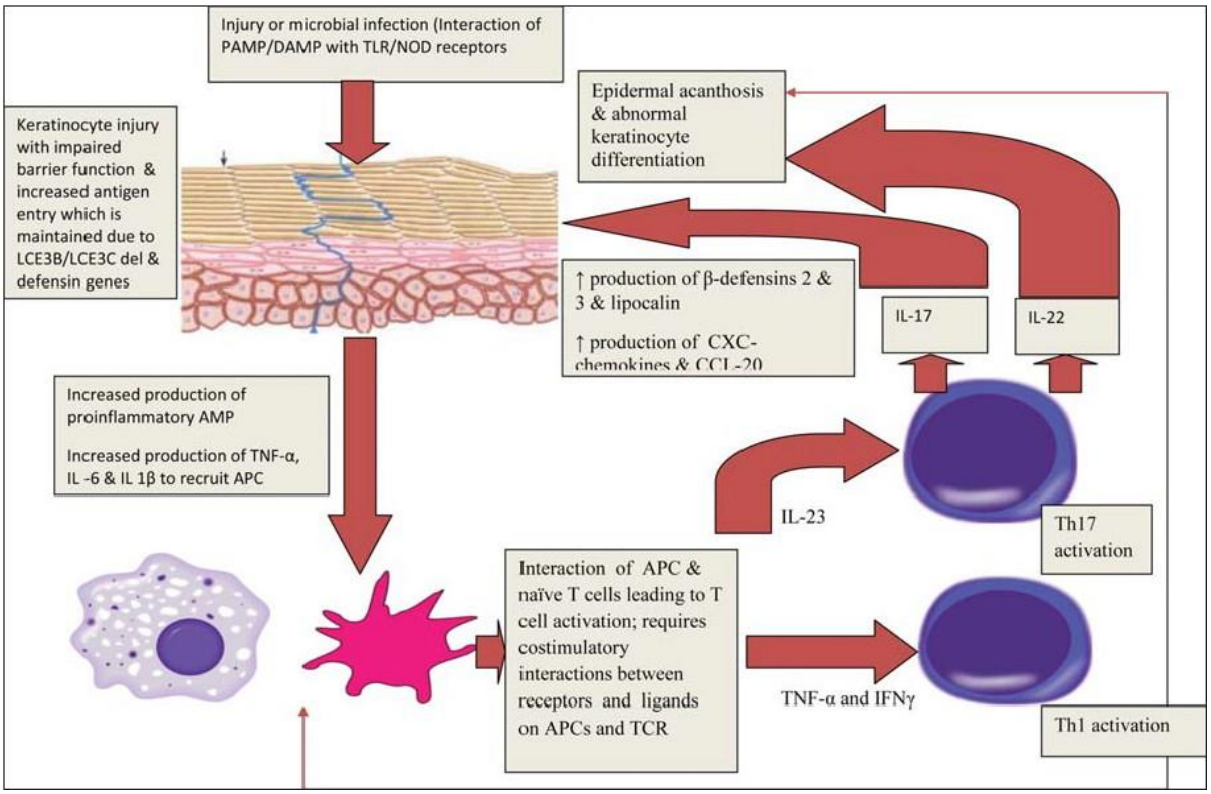


Figure.3b.2.3.Pathogenesis of psoriasis

Once the APCs engulf the inciting antigen, they migrate to the local lymph nodes where they interact with naïve T-cells, resulting in T-cell activation. This process requires interaction between the major histocompatibility complex antigens on APCs with the T-cell receptors. In addition, costimulatory interactions between receptors and ligands on APCs and TCR are important. These include interaction of lymphocyte function antigen (LFA)-3 and CD2; between intercellular adhesion molecule-1 and LFA-1; and between B7 and CD28. [67] Activation of such naïve T cells to pathogenic T cells is facilitated by the presence of polymorphisms in IL-23 genes and HLA-C*06. Sustained activation of HLA-C*06 restricted immunodominant epitopes could lead to antigen specific activation of CD8+ T cells, further amplifying the production of TNF-α and IFN-γ, although such a subtype of T cells has not been identified. Once the T cells are activated, both CD4+ and CD8+ T cells infiltrate the skin and secrete Th1 and Th17 cytokines which activate the keratinocytes. Together with IL-1 and TNF-α from keratinocytes, Th17 cytokines and IFN-γ increase expression of antimicrobial peptides (AMPs). This leads to a vicious positive feedback cycle where initial activation of keratinocytes promotes immune system activation, which in turn activates the keratinocytes and is responsible for the chronic nature of the disease. Since Peroxisome proliferator activated

receptors (PPAR) β/δ (PPAR β/δ), [one of three PPAR isoforms], is a key regulator of glucose and lipid metabolism, its upregulation in psoriasis may partly explain the association with metabolic syndrome.

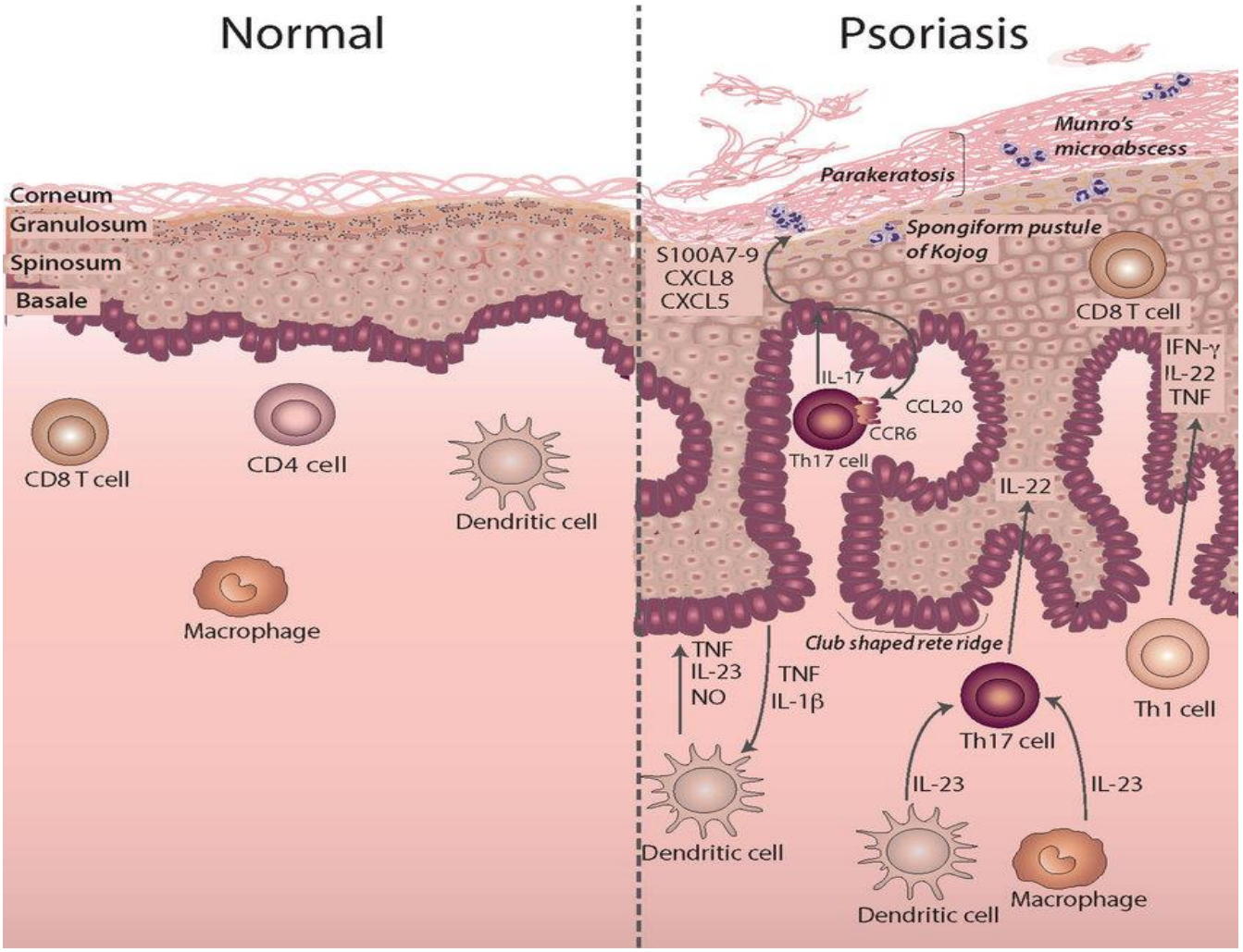


Figure.3b.2.4.Pathogenesis of psoriasis

3b.2.6.Clinical Symptoms and Signs [12]:

- Erythema
- Scaling
- Itching
- Thinkning

Signs and phenomenon:

- With careful scratching, small silvery-white lamellar scales come off, more or less as from a solidified candle strip (candle grease sign)
- Auspitz sign: Removal of this epithelial layer reveals punctuate bleeding because of a lesion of the capillaries running out into the tips of the papillae.
- Koebners phenomenon: If the skin of a psoriatic patient is irritated (e.g. scratching) in the phase of an acute episode of eruption, a new psoriatic focus is formed on the floor of this epithelial lesion.

3b.2.7.Clinical features Types[58] :

Plaque Psoriasis:

This is common type and its lesions are deeper pink in colour.

As the plaques grow in size, they can merge to form annular (ring-shaped) and gyrate (coined) forms. The most characteristic feature is silvery scale. The top scales lift away easily but deeper scales stick together, and when removed, the exposed skin leaves punctuate bleeding points. This is known as Auspitz sign.

Scalp psoriasis :

It is well-defined pale red plaques with a thick surface of silvery scales are seen. These may become confluent and the entire scalp can be involved.

Flexures psoriasis

Psoriasis in flexures, especially under the breasts, and in the natal cleft and perineum can appear different from plaques elsewhere. The scale is usually reduced or absent, leaving shiny deep pink plaques, which may fissure in the depth of the skin crease.

Palmar plantar psoriasis :

Psoriasis can affect the hands and feet and can be difficult to distinguish from contact dermatitis. The fissure occurs especially over the finger tips and heels, the lesion may very painful and slow to heal.

Guttate Psoriasis:

Guttate psoriasis occurs in 2% of patients with psoriasis who are usually younger than 30 years, and is characterized by round 1-to 10-mm, salmon-pink papules (“dew-drops”) with a fine white scale In many cases, it is preceded by a streptococcal throat (strep throat) or sinus infection; however, the pathophysiologic association between the infection and disease is not clearly understood.

Pustular Psoriasis:

It is severe form of disease in which the lesions consist of small superficial pustules which may appear on a plaque type of psoriais.

Psoriasis erythroderma :

The psoriasis may extend to involve the entire body surface and present as generalized redness and scaling all over the body with chills and rigors.

Nails psoriasis :

The fingernails and toenails may show dystrophic changes of psoriasis. Pitting is the commonest nail change, the whole of the nail may loosen and become raised from the nail bed.

3b.2.8.Complications:

Complications of psoriasis may include the following: Secondary infections, Psoriatic arthritis, possible increased risk of lymphoma, cardiovascular disease, ischemic heart disease, and Mitral valve prolapse. Among these, Psoriatic arthritis is a major complication.

Psoriasis Arthropathica:

In a little fraction of psoriatic patients, there is involvement of the joints similar to rheumatoid arthritis. The joints of the fingers, ankles, feet, knees and sacro-iliac are affected; these joints are swollen and painful. The psoriatic eruption and the participation of the joints may increase or decrease simultaneously. Nail changes are regularly present .Radiological changes are osteoporosis followed by increased density, decreased joint space.

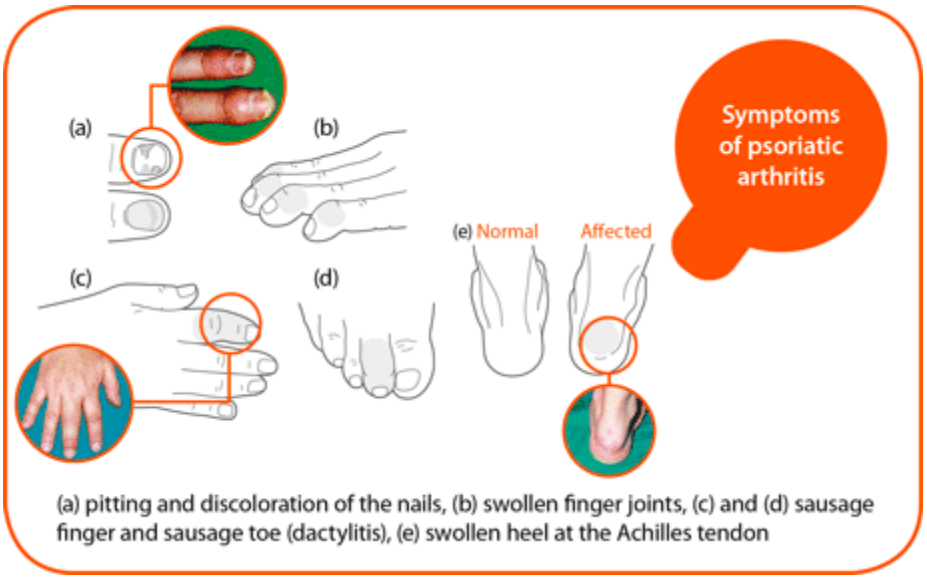


Figure.3b.2.5. Symptoms of Psoriatic arthritis

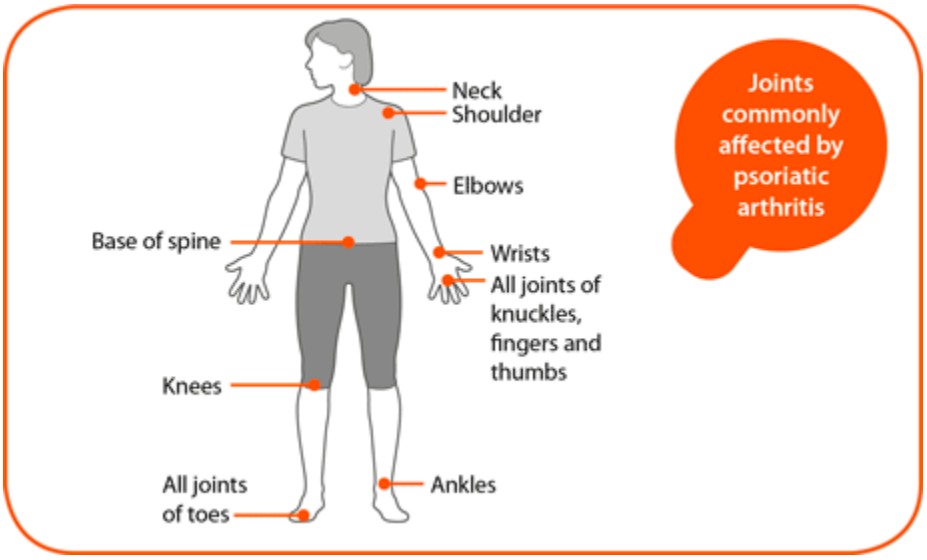


Figure 3b.2.6. Joints affected in Psoriatic arthritis

3b.2.9.Diagnosis of psoriasis:

There are no laboratory tests which will positively identify psoriasis. The blood count, Urine analysis, ESR and other hematologic chemical and serologic studies are within normal limits in most cases of psoriasis.

The diagnosis of psoriasis is based upon:

1. Family history
2. Distribution -scalp, upper limb, lower limb, the front of the legs, front and back trunk and nails.
3. scaling
4. The candle – grease sign.
5. Auspitz sign (Complete removal of a scale produces pin-point bleeding)
6. Koebner's phenomenon
7. Little or no itching
8. Previous attack
9. Seasonal variations.

3b.2.10.DIFFERENTIAL DIAGNOSIS[58]

Nummular eczema

Rounded, circular desquamative **erythematous** lesions covered with vesicles, crusts, and scales, very itchy. Patients have whether atopic or allergic diathesis. Epicutaneous allergy tests are frequently positive.

Pityriasis rubra pilaris

In typical cases follicular papules and infiltrating scales are observed as well as typical hyperkeratosis.

Lichen simplex chronic

This disease shows dry and itchy oval **plaques** and resembles psoriasis as a shape but not have silvery scales Auspitz and candle signs. And shows violaceous tint.

Pityriasis alba

It shows a white plaque, like psoriasis but have not an erythema. It has been seen only face. Psoriasis usually affects more than one area of the body. Red skin covered with greasy-looking white or yellowish scales.

MODERN TREATMENT AVAILABLE FOR PSORIASIS[12]

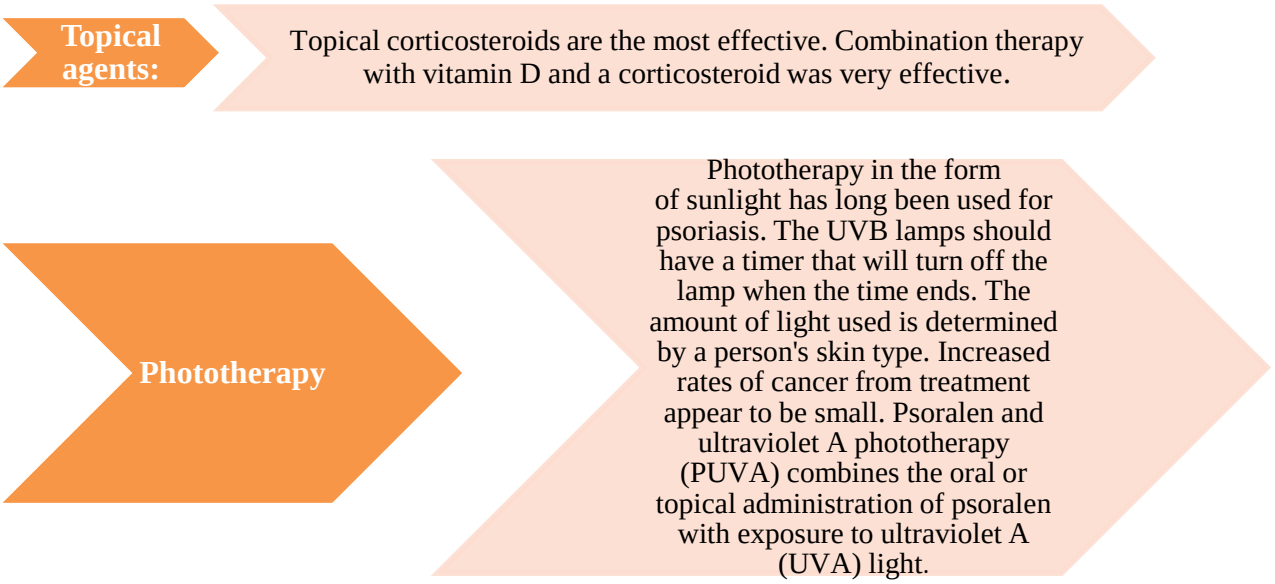


Figure 3b.2.7.Modern treatment for Psoriasis

Drug involved	Key immunologic step inhibited
Methotrexate	Decreases IL-22 levels
Cyclosporine	Decreases IL-15 mediated rise in IL-17 levels
Infliximab, Etanercept, Adalimumab, Golimumab, Certolizumab	TNF-α inhibition
Alefacept	T cell inhibition by blocking the interaction between LFA-3 and CD2
Efalizumab	T cell inhibition by preventing interaction between LFA-1 and ICAM-1
Abatacept	T cell inhibition by inhibiting the binding of CD28 to CD80/CD86
Ustekinumab, Briakinumab, Apilimod	Anti IL 12/23 antibodies
Secukinumab, Ixekizumab, *Brodalumab	IL-17/IL-17R* inhibitors

TNF-α: Tumour necrosis factor-α, LFA: Lymphocyte function antigen, ICAM: intercellular adhesion molecule, CD: cluster of differentiation

3c..DRUG REVIEW

3c.1.INTERNAL MEDICINE

The Siddha system of medicine is 32 forms of internal medicine were described in Siddha text. Kudineer (Decoction) is the one form of internal medicine in which powdered plants or parts of plants added with specific quantity of water prescribed, be boiled upto *1/4,1/8,1/16,1/24* th of the initial quantity and taken after filtering it or prepared in a specific process if mentioned. Decoctions are water based extracts of herbal drugs which are easily absorbed into the body and enter into the blood stream quickly which gives faster action than other forms of medicine.(gets assimilated within an hour).The input water should be pure and without hardness. Depending upon the characteristic feature of the ingredients they may be made into separate pre-mix and blended together. They also should be used within three hours.

3c.1.1.Chemical changes during the preparation of kudineer :

The raw drug components when heated with water two types of changes are taking place hydrolytic and pyrolitic changes.The hydrolytic changes include the conversion of esters into alcohols and acid, rearrangement in the chemical structure of the components,better dispersion in the water,removal of the volatile components with steam,imbibitions of the starchy materials ,decomposition of the proteins into peptides, is omerization and structural changes in the active principles like carotenes,chlorophylls,vitamins,etc.In kudineerpreparation, tracing the chemical changes of even the major components during heating is complicated problem. A kudineer is a multi drug-multi component system. Hence changes can be multi-facial. Each chemical changes is directly influenced by temperature/duration of heating/presence of additives/other components/water/alkaline & acidic materials etc. Isomerization , decomposition, polymerization,etc can also take place depending upon the nature of heating. In majority of kudineer preparations, the particle size of raw drug components has been specified indirectly using the words crushed/ powdered / pressed/etc. They may be used as powder,crushed products, heated and powdered materials / pre-extracted solutions, etc.Addition of components, duration of heating etc,. are also to be specific. The period of storage, reheating , preservation methods, etc are clearly directed for each kudineer. [14]

Trail drug :*Parangipattai Kudineer - PPK* (Internal)

Parangipattai Kudineer is one among the poly herbal formulation contains 10 ingredients which is mentioned in Siddha text book of Pharmacopoeia of hospital of Indian medicine. This drug used for all kind of skin diseases, insect bites,etc.

The drug review of *'Parangipattai Kudineer'* is a poly herbal formulation gives evidence for its therapeutic action mentioned in literatures and research studies.

3c.1.2.PROPERTIES OF TRIAL DRUGS [15]:

1.*Parangipattai* :

Botanical name : *Smilax china.Linn*

Family : Smilacaceae

Organoleptic Characters:

Taste : Sweet

Potency : Coolant

Division : Sweet

General Properties:

"Thagam palavaathand thathunattam punpilavai
megang kadikirandhi veelmooland – thegamudan
kuttai pagandhamer kolvamanam pomparangip
pattaiyinai yuchchariththup paar."

- Agathiyar guna sinthamani

2.*Kadugu Rohini* :

Botanical name : *Picrorhiza kurroa.Royle*

Family : Plantaginaceae

Organoleptic Characters:

Taste : Bitter,Spicy

Potency : Hot

Division : Bitter

General Properties:

"Manthanj suramaiyam vayukarap paanaamanj
sernthamalak kattu thirithodam-ponthapottup
punvayiru noyivaipom porkodiye-pethiyundam
thinkaduku rohinikkuth ther."

- *Agathiyar guna sinthamani*

3.*Manjiti :*

Botanical name : *Rubia cordifolia.Linn*

Family : Rubiaceae

Organoleptic Characters:

Taste : Spicy, Bitter

Potency : Hot

Division : Spicy

4.*Mara manjal :*

Botanical name : *Coscinium fenestratum.Colebr*

Family : Menispermaceae

Organoleptic Characters:

Taste : Bitter

Potency : Hot

Division : Spicy

General Properties:

"Azhandrakana moolam arusi yudaney
uzhandra kanachsuramum odunj-suzhandrulley
veerusura mundhaniyum veesumara manjalukkuth
theru mozhiyanamey seppu."

- *Agathiyar guna sinthamani*

5.*Kadukkai :*

Botanical name : *Terminalia chebula.Retz*

Family : Combretaceae

Organoleptic Characters:

Taste : Spicy

Potency : Hot

Division : Sweet

General Properties:

"Thaadai kazuththakki thalu kuriyividap
peedai silipathamur pethimudam-aadaiyottaath
thoolamidi punvaatha sonikaa malaiyiran
daalamidi pomvarikkaa yaal."

- *Agathiyar guna sinthamani*

6.*Thandrikai :*

Botanical name **:** *Terminalia bellerica.Roxb*

Family **:** Combretaceae

Organoleptic Characters:

Taste : Astringent

Potency : Hot

Division : Sweet

General Properties:

"Silanthividam kamiyappun seezhaana megang
kalandhuvarum vathapithang kalo-dalarnthudalil
undrikai veppa muthirapith thunkarakkun
thandrikai kaiyileduth thaal.
Aanipon menik kazhakum oliyumikum
konikkol vathapiththak kolkaipom-thanikai
kondavarkku megamarum koora anarraniyum
kandavarkku vathampom kaan."

- *Agathiyar guna sinthamani*

7.*Vasambu :*

Botanical name **:** *Acorus calamus.Linn*

Family **:** Araceae

Organoleptic Characters:

Taste : Spicy

Potency : Hot

Division : Spicy

General Properties:

"Pambaki nanjar puthappun valividapagang gunmam
soombaa riraththapith thammuga naarramvan soolaisanni
veembaambai kaasam peeliganj silipatham veerirumal
thaambaag kirumi ivaiyeegu maasiva sampinaiye"

- *Therayar gunavagadam*

8.*Sombu :*

Botanical name **:** *Pimpinella anisum.Linn*

Family **:** Apiaceae

Organoleptic Characters:

Taste : Spicy ,Sweet

Potency : Hot

Division : Spicy

General Properties:

"Yoninoi gunmam urutchaimand thamporumal
penamuru kasam peeligamiraip-peenaurai
serkindra vathamuponj seerperiya seeragaththal
mookkuno yilai mozhi."

- *Agathiyar guna sinthamani*

9.*Vembu :*

Botanical name **:** *Azhadirachta indica.A.Juss*

Family **:** Meliaceae

Organoleptic Characters:

Taste : Bitter

Potency : Hot

Division : Spicy

General Properties:

"Kirumikutta mandhan keduvidanjsu rangal
porumiyam soorikaiyin punkal – orumikka
nimbath thilaiyirukka needulakil neengamal
kambath thilaiyirukkak kaan."

- *Agathiyar guna sinthamani*

10.Seendhil :

Botanical name **:** *Azhadirachta indica.A.Juss*

Family **:** Meliaceae

Organoleptic Characters:

Taste : Bitter

Potency : Hot

Division : Spicy

General Properties:

"Seendhir kizhangkarunthath theebanamam megavagai
ponthavuthi rappiththam pongusura-mandham
athisaram veyyakanam aambalanoo yodey
kathividamung kettuvidung kaan."

- *Agathiyar guna sinthamani*

Parangipattaikudineer is a polyherbal Siddha formulation containing 10 ingredients of plants origin their specific and individual locality names, action, phytochemistry and siddha medicinal uses are tabulated below in Table.

Table.3c..1.Information about ingredients of Parangipattai kudineer[16]

S. No	Botanical name	Tamil name/ English name	Parts used	Phytochemistry	Action	Medicinal uses in Siddha
1.	*Smilax china.Linn*	*Parangipattai /China root*	Root	Flavonoids, Saponins, Sterols, Tannins, Proteins And Carbohydrates	Alterative,Anti syphilitic, Depurative, Aphrodisac	Skin diseases, Inflammations, Diabetic
2.	*Picrorhiza kurroa.Royle*	*Kadugu Rohini/ Picrorhiza*	Root	Pikuroside,Kutkoside, veronicoside, Phenol Glycosides	Anthelmintic, Stomachic, Cathartic, Antiperiodic	Skin diseases, Ulcer
3.	*Rubia cordifolia.Linn*	*Manjitti/Indian madder*	Root	Purpurin,Alizarin, Mollugin,Manjistin	Emmenagogue	Skin diseases, Wound, Inflammation, Diabetic
4.	*Coscinium fenestratum.Colebr*	*Maramanjal/ Tree-Turmeri*	Bark	Berberine, Flavonoids, Sitosterol	Tonic, Stomachic, Febrifuge	Skin diseases, Wound, Inflammations
5.	*Terminalia chebula.Retz*	*Kadukkai/ Chebulic Myrobalan*	Fruit	Chebulinic acid, Tannic acid,Ellagic acid, 2,4 Chebulyi–β-D-Glucopyranose, Gallic acid, Ethyl Gallate,Punicalagin	Tonic Astringent, Stomachic, Laxative	Blood purifier,Skin diseases, Nervous disorder
6.	*Terminalia bellerica.Roxb*	*Thandrikai/ Belleric Myrobalan*	Fruit	Ellargic Acid, Gallic Acid,Tannins,Ethyl Chebulaginic Acid, β-Sitosterol,	Tonic,Laxative ,Expectorant, Astringent	Wound Ulcer Brain tonic

7.	*Acorus calamus.Linn*	*Vasambu/ Sweet-flag*	Root	Methyleugenol, Asaronaldehyde, Terpinolene	Anthelmintic, Antiperiodic, Stomachic, Disinfectant Germicide	Carminative, Emetic, Inflammations
8.	*Pimpinella anisum.Linn*	*Sombu/ Anise seeds*	Seed	Eugenol transanethole, Anisaldehyde, Estragole, Coumarins,Scopoletin,Umbelliferone, Estrols, Terpene, Hydrocarbons	Carminative Stomachic	Carminative , Disinfectant, Sleeplessness, caugh
9.	*Azhadirachta indica. A.Juss*	*Vembu/ Neem tree*	Bark	Nimbidin And Polysaccharides, Margolone, Margolonone And Isomagolonone	Tonic, Antiperiodic, Astringent	Skin diseases, Fissure in foot
10.	*Tinospora cordifolia. Miers*	*Seendhil/ Gulanchatinospora*	Stem	Tinosporin,Giloinin, Berberine, Glucoside.	Tonic, Antiperiodic, Alterative Demulcent	Wound Ulcer, Inflammations

3c.1.3.Pharmacological activity of herbs in Parangipattai Kudineer :

The efficacy of all ingredients of Parangipattai Kudineer was proved through the following research studies.

Smilax china.Linn :

Ethyl acetate fraction of *Smilax china* rhizome showed good ***anti-psoriatic activity*** in the mouse tail test, ***anti-proliferent activity*** and nitric oxide inhibition assay. The plant *Smilax china* rhizome possesses anti-psoriatic activity which is in agreement with its traditional use . *Smilax china* has ***anti-inflammatory activity***. Its decoction (90 and 180 mg/kg; p.o) could significantly inhibit inflammatory swelling on adjunctive arthritis mouse· The methanol extract of *Smilax china* exhibit antimicrobial activity. In vitro antimicrobial activity of *Smilax china* was reported·

Picrorhizakurroa.Royle:

Immunomodulatory activity:

The effect of an ethanolic extract of root of the *Picrorhizakurroa.Royle*was studied on delayed type hypersensitivity, humoral responses to sheep red blood cells, skin allograft rejection, and phagocytic activity of the reticuloendothelial system in mice

Anti-inflammatory activity:

Picrorhiza kurroa.Royle's root has apocynin. Apocynin concentration dependently inhibited the formation of thromboxane A2, where as the release of prostaglandins E2 and F2 was stimulated. Apocynin inhibited arachidonic acid induced aggregation of bovine platelets, possibly through inhibition of thromboxane formation. The rhizome of *Picrorhiza*is used to treat inflammatory diseases as a traditional medication.

Anti-diabetic activity:

Extract of *Picrorhiza* was found to lower blood glucose in laboratory animals. Chronic administration of the extract significantly reduced blood sugar in alloxan-induced diabetic rats for 10 days. The extract was also used to reduce the increased blood urea nitrogen and serum lipid peroxides in alloxan-induced diabetic animals and to inhibit the body weight reduction and leukopenia induced by alloxanadministration.

In the streptozotocin induced diabetic rats, treated with a gavage of ethanol extraction of *Picrorhiza* herbal formulation. It reduced NADPH - oxidase dependent superoxide generation and decreased expression of malondialdehyde and advanced oxidation protein products in diabetic kidney. So, extraction of *Picrorhiza* improves diabetic nephropathy through inhibition of redox sensitive inflammation.

Rubia cordifolia.Linn:

***Anti-Inflammatory Effect*:**

Rubia cordifolia, Linn. (Indian Manjishtha), was studied for the anti-inflammatory effect in rats with carrageenan paw oedema

Anti-bacterial Activity:

The anti-bacterial activity of the extracts of rubia cordifolia root was significantly active against *B. subtilis* and *S. aureus* compared with streptomycin and penicillin G used as standards.

***Anti-proliferating Property*:**

Ethyl acetate fraction of the root of Rubia cordifolia.L inhibits keratinocyte proliferation in vitro and promotes keratinocyte differentiation in vivo

Anti-adipogenic activity of 2-carbomethoxy-2, 3-epoxy-3-prenyl-1, 4-naphthoquinone (CMEP-NQ) isolated from the roots of *Rubia cordifolia*.L., its effects on cell viability, apoptosis, and adipogenesis in 3T3-L1 preadipocytes were investigated.

Coscinium fenestratum.Colebr :

immunomodulatory activity :

The assessment of immunomodulatory activity of ethanolic extract (Crude extract), alkaloid fraction and non-alkaloid fraction of stem bark of *Coscinium fenestratum* was carriedout by performing hemagglutinating antibody titer (H.A.)

Anti-Depression:

Coscinium fenestratum is a common medicinal plant widely used in the Indochina region, but scientific data on its safety is very limited. Oral administration of plant alcoholic extract at dosages of 5, 10 and 20 mg/kg BW for 14 days increased the rats body weight and decreased the neuron density in the cerebral cortex, hippocampus and striatum. The plant extract significantly increased stereotyped behavior in licking but did not cause anxiolytic activity, anti-depression, sensory motor co-ordination impairment and ataxia.

Terminalia chebulla.Retz:

Pharmacological investigations for ***antimutagenic, immunodulatory*** *effect,* ***antibacterial***, ***antifungal*** of different biological activities of *Terminalia chebula*in various in vivo and in vitro test models have been carried out based on the presence of chemical ingredients. The ethanolic extract of *Terminalia chebula*fruits possesses analgesic and ***anti-inflammatory*** activities in mice and rats at the doses of 250 mg/kg and 500 mg/kg and, 300 mg/kg respectively

Terminalia bellerica.Roxb:

Pharmacological activities such as ***anti-microbial, anti-oxidant,immumomodulatory, anti-spasmodic*** of different biological activities of of Terminalia bellerica in various in vivo and in vitro test models have been carried out based on the presence of chemical ingredients

Acorus calamus .Linn :

Anti-inflammatory:

Anti-inflammatory activity on keratinocyte hacat cells HaCaT cells induced the pro-inflammatory cytokines, interleukin-8 (IL-8) and interleukin-6 (IL-6) expressions after treatment with polyI:C or PGN. ACL inhibited the expression of IL-8 and IL-6 RNA and protein levels, and attenuated the activation of NF-κB and IRF3 after polyI:C treatment. ACL also inhibited expression of IL-8 and activation of NF-κB following PGN induction. ACL inhibits the production of pro-inflammatory cytokines through multiple mechanisms and may be a novel and effective anti-inflammatory agent for the treatment of skin diseases.

***Anti-cellular* and *immunosuppressive* properties** :

Modulation of immune response to alleviate disease has been of interest since long. Plant extracts have been widely investigated for possible immunomodulatory properties. The anti-cellular and immunomodulatory property of ethanolic extract of*Acorus calamus* rhizome has been evaluated. This extract inhibited proliferation of mitogen (phytohaemagglutinin; PHA) and antigen(purified protein derivative; PPD)-stimulated human peripheral blood mononuclear cells (PBMCs). In addition, *A.calamus*extract inhibited growth of several cell lines of mouse and human origin. It also inhibited production of nitric oxide (NO), interleukin-2 (IL-2) and tumor necrosis factor-a (TNF-a). Intra cytoplasmic interferon-gamma (IFN-gamma) and expression of cell surface markers,CD16 and HLA-DR, on human PBMC, were not affected on treatment with *A. calamus* extract but CD25 expression was down regulates.

Pimpinella anisum.Linn:

Pharmacological properties of *Pimpinella anisum* such as ***antimicrobial, antifungal, antiviral, antioxidant,*** and insecticidal effects have been reported of aniseeds

Azhadirachta indica.A.Juss:

The extracts showed potential ***antimicrobial activities*** against thirteen different strains of microorganisms. Secondly, they were screened in vitro for cytotoxicity test by brine shrimp lethality bioassay and results illustrated significant ($p<0.05$) cytotoxicity against Artemiasalina. To test the analgesic properties of ethanol extract of Azadirachta indica, hot plate and acetic acid induced writhing methods were used. At two different doses (250 and 500 mg/kg body weight), the analgesic tests were performed on Swiss Albino mice. Also, the anti-inflammatory tests were performed by carrageenan induced paw edema method on long Evans rats at the two different doses of 250 and 500 mg/kg body weight using ethanol extract. Our results indicated that Azadirachta indica possesses remarkable **analgesic** and ***anti-inflammatory activity***.

Tinospora cordifolia.Miers:

Tinospora cordifolia has an importance in traditional medicine used for ages in the treatment of fever, jaundice, chronic diarrhea, cancer, dysentery, bone fracture, pain, asthma, skin disease, poisonous insect bite, snake bite, eye disorders. Pharmacological activities such as ***antimicrobial, antioxidant, immumomodulatory,antispasmodic*** of different biological activities of *Tinospora cordifolia* in various in vivo and in vitro test models have been carried out based on the presence of chemical ingredients

3c.2.EXTERNAL MEDICINE

The Siddha system of medicine is 32 forms of external medicine were described in Siddha text. Medicated oils are prepared by extracting drug substances in oil. Shelf life of medicated oil is one year. Apart from vegetable oil animal fats are also used.

In *thylams,* the medicinal principles of the raw drugs are directly or indirectly dissolved in the oils.Cleanliness, purity of the drugs, good storage conditions, free from microbial and other contaminations are the pre-conditions to be satisfied in the preparation of the *thylams* for maintaining the quality of the oil, otherwise the peroxide formation, rancidity and hydrolytic degradation will result in t*hylams*. There are two general methods for the preparation of the *thylams* either by directly heating the oil with raw drugs after proper grinding or extracting the active principles of the drugs with water or milk and then from that, the thylam is prepared.In the first method the active principles of the drug get dissolved in the oil and it is absorbed either externally or internally depending upon its application. In the second method, all the required heat and hydrolytic changes will be taking place when the raw drugs are extracted as kudineer and from that concentrate; the active principles get dissolved into the oil[14].

Trail drug :*Sivappu thylam* (External)

Sivappu thylam is one among the poly herbal formulation contains 8 ingredients which is mentioned in siddha text book of Pharmacopoeia of hospital of Indian medicine. This drug used for all kind of skin diseases. The drug review of *'Sivappu thylam'* , is a poly herbal formulation gives evidence for its therapeutic action mentioned in literatures and research studies.

3c.2.1.PROPERTIES OF TRIAL DRUGS [15]:

1.*Pungan Ver* :

Botanical name : *Pongamia pinnata Pierre*
Family : Fabaceae

Organoleptic Characters:

Taste : Bitter, Astringent

Potency : Hot

Division : Spicy

General Properties:

"Punginvidhai karkirandhi punkarappan kathezhuchchi

Angasanni kannoykkum aambethi-yungkattum

Kaatuppung kin vithaikku kandathey marsorimeip

Poottuppang kinvaayvum pom."

- *Agathiyar guna sinthamani*

2.*Manjiti* :

Botanical name : *Rubia cordifolia.Linn*

Family : Rubiaceae

Organoleptic Characters:

Taste : Spicy, Bitter

Potency : Hot

Division : Spicy

3. *Nannari :*

Botanical name : *Hemidesmus indicus R.Br*

Family : Asclepiadaceae

Organoleptic Characters:

Taste : Sweet, Bitter

Potency : Coolant

Division : Sweet

General Properties:

"Salathodam piththamathi thaagam uzhalai

Salameru seethaminnaar thanjoo-dulagamathir

Sonnamathu megam pun suramivaiye laamozhikkum

Menmathura nannari ver."

-Therayar gunavagadam

4. *Manjal Mezhugu (Cera wax) :*

General Properties:

"Araipakka vatha mathaippaiya moothai

Kuraivindhi thazhnoy thelkooli-karaiyaip

Puzhukedukka vangamuru punnidippun deeppun

Mezhugedukka vaangalu mei."

- *Pathartha guna sinthamani*

6. ***Vellai Kungiliyam.:***

Botanical name : *Vateria indica Linn*
Family : Dipterocarpaceae

Organoleptic Characters:

Taste : Bitter

Potency : Hot

Division : Spicy

General Properties:

"Vellai yaliththa virananaa pikkamalath

Thollaivira nammegandh thorrukinum- ulley

Varuvarasanaimerpun varinunj suvethach

saruvarasa merpazhiyaich chaarru."

-Therayar gunavagadam

6. *Chevvallikkodi :*

Botanical name : *Dioscorea purpurea*
Family : *Dioscorea*ceae

Organoleptic Characters :

Taste : Sweet

Potency : Coolant

Division : Sweet

General Properties :

"sevvalli yinkodikkuch sediththa kuttamodu

Kavvu kurainoyi karappanum-ivvulakil

Maaney ! kudalvatham valla vaduvanudan

Aanaparu moolamumpom aay."

- Agathiyar guna sinthamani

7. *Surul Pattai :*

Botanical name : *Cinnamomum verum.Juss*
Family : Lauraceae

Organoleptic Characters:

Taste : Spicy, Sweet

Potency : Coolant ,Hot

Division : Sweet,Spicy

General Properties:

"Thathunattam pethi saruvavisam aagiyanoyi

Poothakira kanjsilandhip poochchividanj-saathividam

Aattumiraip podirumal aagiyanoyik koottamara

Oatttumila vangath thuri."

- Agathiyar guna sinthamani

8. *Coconut Oil* :

Botanical name : *Cocos nucifera Linn*
Family : Arecaceae

Organoleptic Characters:

Taste : Sweet

Potency : Coolant

Division : Sweet

General Properties:

"Thengayi neyyathanaar riyaal varupunpom

Paangaakak koondhar padandheru-neengadha

Palladiyin noyum padatha maraisirangum

Allarap pomen rari."

- Agathiyar guna sinthamani

Table.3c.2.1.Information about ingredients of *Sivappu thylam*[17]

S. No	Botanical name	Tamil name/ English name	Parts used	Phytochemistry	Action	Medicinal uses in Siddha
1.	*Pongamia pinnata Pierre*	*Pungu/Indian beech*	Root	Demethoxy-Kanugin, Glabrin, Kanugin,Karangin, flavonoids, Flurophenylalaline, Vinblastin, incristine (Sulphate),Teniposide, Fluoxetine	Astringent, Alterative, Anti-septic, Parasiticide	Skin diseases, Inflammations Diabetic
2.	*Rubia cordifolia.Linn*	*Manjitti /Indian madder*	Root	Purpurin,Alizarin,Mollugin,Manjistin[23]	Emmenagogue	Skin diseases, Wound, Inflammation, Diabetic

3.	*Hemidesmus indicus R.Br*	*Nannari / Indian Sarasaparilla*	Root	Glucose hemidesmol, 2hydroxy-4-methoxy benzaldehyde, glucoside, resin acid, sterol, and tannins	Alternative Tonic Demulcent Diuretic Diaphoretic	Skin diseases Inflammation Syphilis Urinary disorders
4.	Manjal mezhugu	*Cera wax*	Wax	Cerotic Acid Myricin	Demulcent	Skin diseases, Wound, Inflammations
5.	*Vateria indica Linn*	*Kungiliam /Sal tree*	Resin	Triterpene Hydrocarbons, ketones, sesquiterpenes	Stimulant Diuretic	Skin diseases, Nervous disorder Arthritis
6.	*Dioscorea purpurea / Dioscorea alata*	*Chevvallikodi*	Bark	Alkaloids, Carbohydrates, Flavonoids, Glycosides, Phenols, Saponins, Tannins, Terpenoids, Anthraquinones, And Triterpenoids	Anthelmintic	Skin diseases
7.	*Cinnamomum verum.Juss*	*Vasambu/ Sweet-flag*	Bark	Camphene, Sabinene Myrcene, Limonene Terpinolene, Eugenol	Stimulant Carminative	Insecticidal Inflammation
8.	*Cocos nucifera Linn*	*Thengai / Coconut*	Oil	Phenols, Tannins, Leucoanthocyanidins, flavonoids, Triterpenes, Steroids	Stomachic Diuretic Demulcent	Insecticidal Disinfectant Appetizer

3c.2.2.Pharmacological activity of herbs in *Sivappu thylam* :

The efficacy of all ingredients of *Sivappu thylam* was proved through the following research studies.

1.Pongamia pinnata Pierre[19] :

The plant shows the presence of many chemical constituents like alkaloids, tannins, steroids, glycosides, demethoxy-kanugin, glabrin, kanugin, karangin, flavonoids and fixed oils which are responsible for varied pharmacological and medicinal properties like *Anti-inflammatory activity, Anti-pyretic action,Anti-microbial activity,Anti-diarrhoeal action, Anti-viral activity, Anti-hepato-protective activity, Anti-filarial activity, Dyspepsia, Gonorrhea, Leprosy, Anti-hyperglycemic activity, Antilipidperoxidative activity, Anti-hyperammonemic activity, Antioxidant activity*.

2.Rubia cordifolia.Linn [16]:

Anti-Inflammatory Effect:

Rubia cordifolia, Linn. (Indian Manjishtha), was studied for the anti-inflammatory effect in rats with carrageenan paw oedema

Antibacterial Activity:

The antibacterial activity of the extracts of Rubia cordifolia root was significantly active against *B. subtilis* and *S. aureus* compared with streptomycin and penicillin G used as standards.

Anti-proliferating Property:

Ethyl acetate fraction of the root of Rubia cordifolia.L inhibits keratinocyte proliferation in vitro and promotes keratinocyte differentiation in vivo

Anti-adipogenic activity of 2-carbomethoxy-2, 3-epoxy-3-prenyl-1, 4-naphthoquinone (CMEP-NQ) isolated from the roots of *Rubia cordifolia*.L., its effects on cell viability, apoptosis, and adipogenesis in 3T3-L1 preadipocytes were investigated·

***3.Hemidesmus indicus R.Br* :**

Anti-inflammatory activity[20] :

Ethyl acetate root extract of HI exhibited anti-inflammatory activity in acute and subacute inflammation evident from the significant inhibition of inflammation caused by carrageenan, bradykinin, S-hydroxy tryptamine in rats. The extract was less active than phenylbutazone. HI root aqueous extract showed sufficient anti-inflammatory activity compared to diclofenac sodium gel

Anti-cancerous activity[21] :

Roots of HI exhibit protective activity against hepatocarcinogenesis and other cancers

Anti-arthritic activity [22]

HI root display protective activity against arthritis, probably assigned by the presence of terpenes, sterols, and phenolic compounds in hydroalcoholic root extract and ethyl acetate fraction. These fractions showed higher anti-arthritic activity than chloroform and residual fraction

4.*Manjal mezhugu (Cera wax)[23]* :

Yellow Wax. A peculiar, concrete substance, preparedby ApismellificaLinne.Ethanol extracts of propolis (EEP) have shown antibacterial activities. Therefore, propolis might be useful as antibacterial especially against Bacillus subtilis, MRSA, Micrococcus, Escherichia coli, Pseudomonas aeruginosa and Proteus vulgaris.

5.Vateria indicaLinn[24] :

Vateria indica Linn. resin extract possess significant Anti-inflammatory, Anti-ulcer.

6.Dioscorea purpurea/ Dioscorea alata[25] :

Antioxidant Activity and Anti-bacterial activity :

Extract of D. alata exerts antioxidant and antibacterial activities. Antioxidant activity investigated by DPPH free radical scavenging assay, the IC50 value of plant extract was 24.99µg/mL. Significant absorption of extract (1.317 of 1mg/mL) showed the ferric reducing activity. Extract showed significant zone of inhibition in antibacterial activity test. The presence of myricetin along with other detected polyphenols might contribute to antioxidant and antibacterial activities.

7.Cinnamomum verum.Juss[26]

Antimicrobial :

Cinnamomum extract and oil possess various antimicrobial activities against several bacteria and fungi etc,.

8.Cocos nucifera Linn[27] :

Anti-inflammatory :

A study using animal models of inflammation (formalin test and subcutaneous air pouch model) showed that aqueous crude extracts of C. nucifera var. typica (50, or 100 mg/kg) significantly inhibited (Po0.05) the time that animals spent licking their formalin-injected paws and reduced inflammation induced by subcutaneous carrageenan injection by reducing cell migration, extravasation of protein, and TNF-a production.

3D.YOGAM REVIEW

***3d..1..Karpa Yogam*:**

The famous verses from ***Agathiyar Gnanam,*** a Siddha literature speaks about treating the mind as follows;

"*If the mind is good then no need of chanting*
If the mind is good then no need of breathing exercise
If the mind is good then no need of retention of inspired air
If the mind is good the body is good"

A Life free of ailments especially from life style disorders, a proper co-ordination over the psychic stage, psychosomatic stage and organic stage towards the available holistic health and Positive thinking are attained by Yogic practices. The integrated approach of Yoga therapy (IAYT) is the need of the hour in maintaining sound physical, mental and social well being of people globally.

The concept of Ashtanga Yogam mentioned in *Thirumandhiram*, a Tamil Siddha literature, have enormous contribution towards holistic health by practising Eight steps of Yoga are outlined here.

"Iyama niyamam ennilaa aadhanam
Nayamuru pranaayaamam prathiyaagaram
Sayamuru dhaaranai dhiyanam samadhi
Ayamurum attangam aavadhu mamae"
-Tamil moovayiram

- Iyamam (Purity of Mind)
- Niyamam (Purity of Action)
- Asanam (Posture)
- Pranayamam (Breathing technique)
- Prathyaharam (Controlling Sense)
- Dharnai (Concentrating Mind)
- Dhyanam (Continuous Contemplation)
- Samadhi (Achieving the Goal, Attaining Godhood)

3d.2.In *Agathiyar Maamunivar Paripooram* 1200 [28]:

Attangam : 8

"Kaanavey attanga mettuk kezhu

---------- *Kaaviyaththai kanduthaerey"* Verse no : 1121

Iyamam : 11

"Thaerappaa thaerndhumanang kandukozhzha

---------- *Naemamadhaith thiramaaikkaney"* Verse no : 1122, 1123

Naemam : 10

"Kaanavey naemamadhu eeranjappaa

---------- *Sugamaga naemavagai paththunjsithey"* Verse no : 1124

Aasanam : 9

"Siththamudan naemavagai paththukkandu ----------

Veththyuzhzha aasandhaa nonbadhappa ----------

Karpoora theebam paarey" Verse no : 1125-1126

Prathiyagaram : 6

"Muththiyudan sivayogath thirundhu kondu

---------- *aaruvagai prathiyagaram paarey"* Verse no : 1128

Thaaranai : 6

"Paaradaa thaaranaithaa naaru vagaithannai

---------- *naruvagai thaaranaithan paarey"* Verse no : 1129

Dhiyanam : 10

"Paarappa aaruvagai thaaranaiyin nindru

Pathivaana athiyanavagai paththung kezhu

---------- vagaiyai kezhey" Verse no : 1130 – 1131

Samathi 5:

"Kezhappaa samadhiyanju nandraai solven

Kirubaiyuzhzha thathvalaya samadhiyondru

---------- *sagalasiththu maadalamey"* Verse no : 1132 – 1133

The above verses are describes about Attangayogam & its divisions, subdivisions.

3d.3.The role of psychoneuroimmunology[29]

Psychodermatology is a relatively new discipline in psychosomatic medicine. It is the interaction between mind and skin. The two disciplines are interconnected at the embryonal level through ectoderm. There is a complex interplay between skin and the neuroendocrine and immune systems. Skin responds to both endogenous and exogenous stimuli. It senses and integrates environmental cues and transmits.

Stress activates 2 major neuronal pathways: the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system. The identification of external stress by the brain results in activation of the paraventricular nucleus of the hypothalamus and locus ceruleus. Corticotropin-releasing factor is secreted from the hypothalamus and transported through portal circulation to the pituitary, where it induces the release of adrenocorticotropic hormone from the anterior pituitary to the general circulation. This results in the secretion of glucocorticoids and catecholamines from the adrenal gland.

Cortisol acts as negative feedback on the hypothalamus and inhibits the further release of corticotropin-releasing factor. The cells of the locus ceruleus activate the sympathetic system, which results in the secretion of epinephrine and norepinephrine.

Both catecholamines and cortisol have potent effects on the immune system. They modulate antigen-presenting cells and macrophages and inhibit their activity and the production of interleukin (IL)-12 and IL-18. They also mediate the differentiation of naive T-helper (TH) cells toward TH2, to the detriment of the development of TH1. This tilts the balance toward humoral immunity and activates B cells, mast cells, and eosinophils, with a consequent increase in allergic inflammatory response. Nerve terminals in cutaneous sensory nerves release neuropeptides, such as calcitonin gene-related peptide and substance P, which have a variety of effects on local inflammatory response; these affect several psychocutaneous disorders.

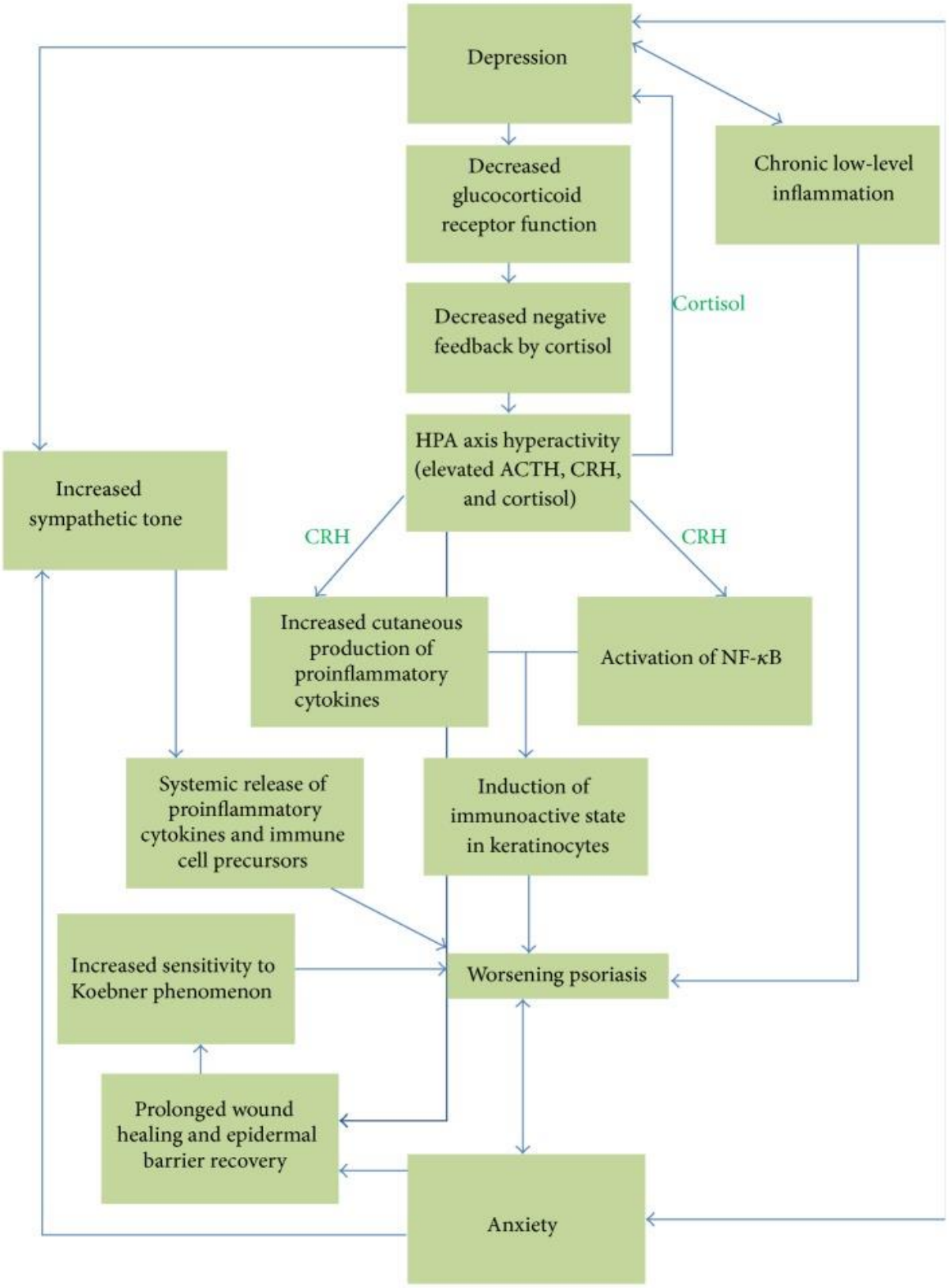


Figure.5a.1.The role of psychoneuroimmunology

Skin is the reflex of mind and so we should treat not only the physical but also treat mind and soul. There by patients are advised to do *yogam* practice.

Asanas like,

- Yogam therapy (Agathavam Ettu)
- Surya namaskaram (Sun salutation)
- Padmasanam (Lotus position)
- Nadi suddhi pranayamam (Alternate nostril breathing practice)
- Paschimottanasanam (Forward bend pose)
- Makarasanam (Crocodile pose) will be given for IPD patients and these are all beneficial to relieve stress and strain.

3d.4..SURYANAMASKARAM[30]:

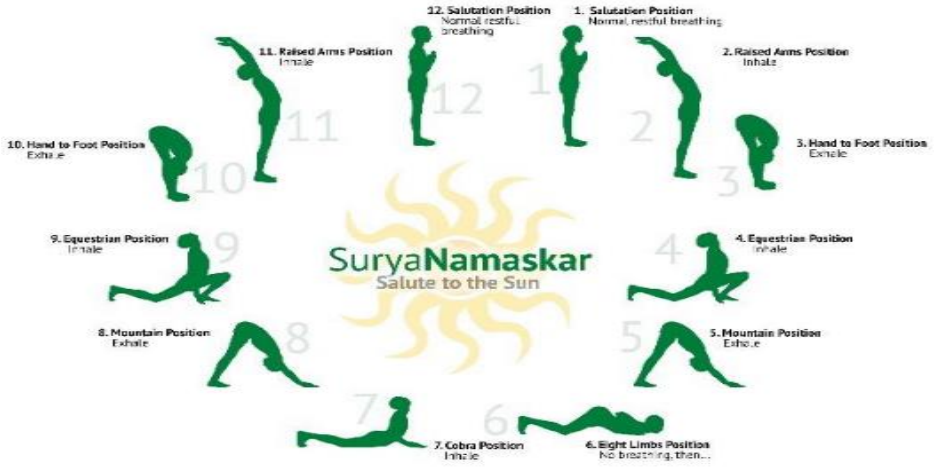


Figure.5a.2.Suryanamaskaram

Surya" means sun and "**Namaskar**" Means Salutation. Suryanamaskar is the complete body workout. It is Very effective in weight loss program. Only in Suryanamaskar (Sun Salutation), there are 12 different yoga poses which give total exercise to the whole body. By practicing the sun salutation regularly, we can become active and strong in our whole life.

Morning is the best time to practice Suryanamskar (Sun Salutation). But don't eat anything for 5 hours prior to Surya Namaskar

Steps for Surya Namaskaram :

Surya Namaskar (Sun Salutation) is the combination of 12 different asanas (Yoga poses).

1. **Pranamasanam** : Stand straight and erect in such a way that your face is in the direction of the sun. Both feet should be touching each other. Bring your hands close to your chest by touching palm to palm called Namaskar (Salutation).
2. **Hastauttanasanam** : Take a deep breath and raise your hand in upward direction.
3. **Padahastasanam**: Now breathe out slowly and bend forward. Hands should be lined with your feet and head touching your knees.
4. **Ashwa Sanchalanasanam** :Inhale slowly and extend the right leg back and drop the knee to the ground. Bend the left knee and hands should be firm with the ground.
5. **Parvatasanam :** During exhaling bring the right leg back to join the left leg. Raise your buttocks upwards forming a triangle.

6. **Ashtanga namaskaram :**Exhale until your feet, knees, hands, chest, forehead touches the ground. Hold the breath.

7. **Bujangasanam :**On inhaling raise your head in an upward direction and bend in the backward direction as much you can. It is called Bhujagasana pose.

8. **Parvatasanam :**Now exhale slowly and make an upward arc

9 .**Ashwa Sanchalanasanam** : Inhale slowly and extend the right leg back and drop the knee to the ground. Bend the left knee and hands should be firm with the ground.

10.**Padahastasanam** : Now breathe out slowly and bend forward. Hands should be lined with your feet and head touching your knees.

11.**Hastauttanasanam** : Take a deep breath and raise your hand in upward direction.

12.**Pranamasanam** : Stand straight and erect in such a way that your face is in the direction of the sun. Both feet should be touching each other. Bring your hands close to your chest by touching palm to palm called Namaskar (Salutation).

Benefits of Surya Namaskar (Sun Salutation) :

- Effective in weight loss.
- Improved digestion and appetite.
- Cures constipation.
- Increases body flexibility.
- Helps to Reduce stress and stay calm.
- It strengthens the arms, back, shoulders and legs, hips, quads and calves.
- It gives physical and mental strength.
- In one word it is one of the excellent asanas for the entire body.

Precaution :

- Pregnant women should not practice Suryanamaskar.
- Those suffering from high blood pressure and hernia should not practice Suryanamaskar.
- During menses, women should avoid Suryanamaskar.
- Those suffering from back pain should take expert guidance. All asana should perform under expert guidance.

3d.5.Padmasanam Yoga (Lotus Pose)[31] :

In Sanskrit, "Padmam" means lotus. Hence padmasana is called the lotus pose.

Figure.5a.3. Padmasanam Yoga

Padmasana Yoga Steps:

Padmasana is quite a difficult asana. Hence it is ideal to perform few preparatory asanas like Pigeon pose or Butterfly pose before performing this asana.

1. Begin by sitting in a cross-legged posture with right leg crossed over your left. Ensure that your hips are higher than your knees.

2. Taking the assistance of your hands, bring your right foot onto the left thigh such that the hell touches the hip joint.

3. Now turn the sole of your foot up, lengthening through your ankle.

4. Once you are comfortable in this position, bring your left foot onto the right thigh with the heel touching the hip joint, sole turned up.

5. Gently press down your ankles to your thighs. Now extend from the base of the perineum, all the way up the length of the spine, with full energy in one go.

6. Now place your hands on the knees. And bring your fingers to Sin mudra, i.e, with the thumbs and index finger forming a circle and the rest of the fingers extended out.

7. Remain in this position for a period of time, taking deep breaths, as many as possible.

8. In case, you experience any difficulty or numbing sensation, go back to the original position immediately.

9. While practising, remember to alternate the lead leg every time you come to this pose.

Padmasana (Lotus Pose) Benefits:

- Padmasana yoga is quoted as the "destroyer of all diseases" in traditional texts.
- Helps to Reduce stress and stay calm.
- Help to stretch the spine,knees and ankles.

Precautions For Padmasana (Yoga Lotus Pose):

- Knee injury or ankle injury.

3d.6.Nadi sudhi Pranayamam(Breathing techniques)[32] :

Pranayamam (Mochu Payirchi)

Pranayamam means Controlling the Prama or breathe . "prana" + "ayama" • Prana = pra (prefix) + an (to breathe, to live) • "prana" is life-force, the cosmic vital energy • "ayama" means to stretch, expand, control • Pranayama is to expand and control prana • Breath is a gross manifestation of prana, usually equated with prana equated with prana • Breathing techniques help control prana in different waysywe may not be able to control it right away,but bybeing able to monitor your breath ,you can literally place your life in your own hands.

If u take in 21,600 breaths a day on average ,you could live for120 years.if u breathe at a faster pace,your lifespan is shortened. When you lessen the number of inhalations,your life spans increasese.breath goes out for 12 inches and goes in only 8 inches-4 inches is ordinarily wasted.while eating 18 inches ,walking 24 inches,running -42 inches,During intercourse and sleeping -50t060 inches are wasted.so our life will be less than 120 years.

The practice of *Pranayama* varies from person to person.

Nadi sudhi: The breath taken by the left nostril is known as Idaikalai and the breath taken by the right nostril is known as Pingalai. Left nostril breath is cooling and Right nostril breath is heat. If we concentrate our breath, it flow any one side of the nostril, at that time other nostril won't

take breath. After sometime the next nostril will take breath and the other wont. Sometimes both of the nostrils will take breath, which is the symptom the breath will going to change to any one nostril. Thus our body heat will be spontaneously balanced by these alternate nostril breathing.

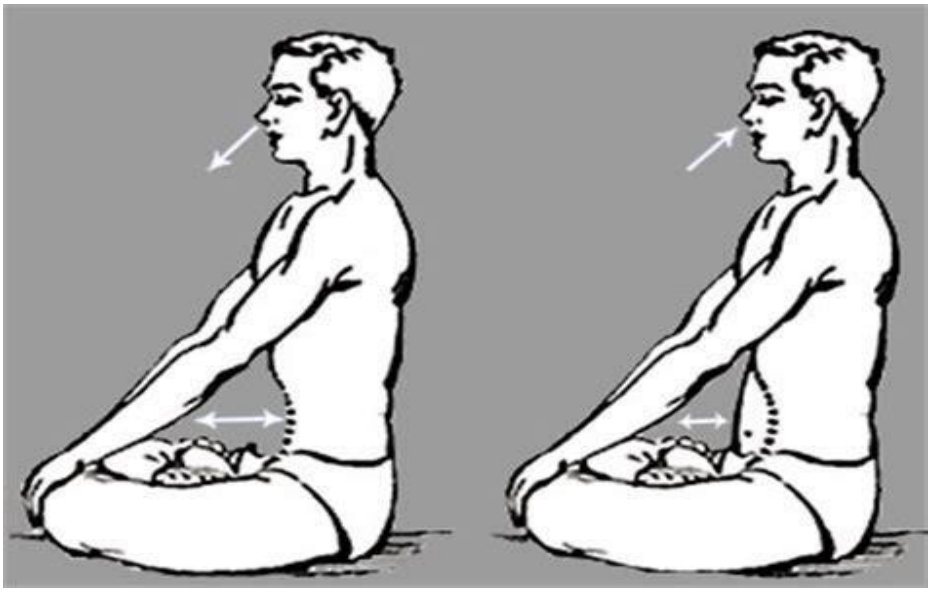


Figure.5a.4. Nadi sudhi Pranayamam

Procedure :

1. Sit in Padmasana
2. Keep the spine erect and your head and neck straight
3. Your eyes should be closed
4. Relax the muscles of the body and become aware of your breath
5. At no point during the exercise should the breath be controlled or forced
6. If you find the Padmasana pose difficult to maintain, you can practice Nadi Suddhi breathing seated on a chairi It is important to make sure that your feet are on the floor and your back is straight throughout the time you are in this posturer
7. With one hand, let your fingers stretch and bend your index and your middle fingers and place them on the palm of your handn
8. Place the thumb on one nostril and the tip of the ring finger against the other nostrili
9. The thumb and ring finger will be used to close alternate nostrils as you breatheh
10. Begin the exercise by blocking your left side nostril and breathe out with your right nostrili
11. Continue to block your left nostril and breathe in using your right nostrili
12. Open your left nostril as you simultaneously cover and block your right nostrili Breathe out slowly using the open left nostrili

13. Once this is done go ahead and breathe in with your left nostril that is opene
14. Close the left nostril and let the air move out through your right nostril that you now leave opene
15. This is considered one cyclel The breathing should be slow and rhythmici
16. Continue breathing this way by opening and closing left and right nostrils and complete ten cycles to begin witht
17. As you advance in your practice, you can increase the duration of each cycle and the number of repetitionsn

As a beginner, Nadi Suddhi pranayama can take a great deal of practice and concentration to mastere Try and focus on the breath to prevent the mind from wanderingn.

Duration:

Ideally, at least 18 to 30 rounds of Alternate Nostril breathing should be performed to maximize the benefits.

Benefits

- As pure oxygenated air is breathed into the lungs with each cycle, the blood gets purified and circulation improvese
- This pranayama helps strengthen the lungs and increases overall lung capacity.
- As circulation improves, energy levels also increases
- Nadi Suddhi pranayama can help with weight loss as it increases the rate of metabolisms.
- It helps calm the nervous systeme
- Regular practice helps reduce stresss
- It can improve mental healtht
- Alternate Nostril breathing can help remove excess body heata
- It can help improve appetitet
- Alternate Nostril breathing can help reduce body odoro
- This type of pranayama breathing is believed to strengthen the immune system and prevent illnessese

Precautions:

- The effects of pranayama breathing on the organs are almost instantaneousu Therefore it is extremely important, to practice pranayama breathing exercises only under the supervision and guidance of a trained yoga instructor.

- There should be no forced or strained breathing during the exercise, as this can prove harmful to the body.

- If during the exercise, you feel your body shaking involuntarily or that your muscles have become tense, stop the exercise and breathe normallyl
- If you suffer from high blood pressure, you should avoid Alternate Nostril breathing.

3d.7.Paschimottanasanam (Seated Forward Bend pose) [33]:

Paschimottanasana is the Sanskrit word. "**Paschima**" means your "**back**" and "**Uttana**" means "**stretching**". It is also known as seated forward bend pose. This asana covers the stretching of the whole body from head to heels.

Figure.5a.5. Paschimottanasanam

Benefits :

- It acts as a *stress reliever.*
- Reduces fatty deposits in the abdomen.
- *Remove anxiety, anger, and irritability.*
- *Calms the mind.*
- Stretches the spine and brings flexibility.
- Good for constipation and digestive disorder.
- Regular practice cure impotency and enhance the sexual power.

- Tones the abdominal-pelvic organs.
- Balance the menstrual cycles.
- This asana is recommended especially for women after delivery.

Steps :

Sit down straight with your legs together by stretching in front of you. keep your head neck and spine erect.

1. Place the palms on your respective knees.
2. Now bend your head and trunk slowly forward to catch the toes with the thumb, index and middle fingers without bending knees.
3. Take a deep breath and exhale slowly. Try to touch your head to your both knees.
4. Bend the arm and try to touch the elbow on the floor.
5. Exhale completely and holding out your breath stay in this posture for a few seconds.
6. After few seconds slowly return to your starting position.
7. breathe normally.
8. Repeat this for 3-4 times.

Precautions :

- Pregnant women should not practice Paschimottanasana.
- A person suffering from slip disc or sciatica problem, asthma should avoid Paschimottanasana.
- Ulcer patient should not practice.

3d.8.Makarasanam (Crocodile Pose) [34]:

Figure.5a.6. Makarasanam

Steps

1. First, lie down on your stomach and stretch your hands forward.
2. Before going to next steps, breathe normally for few seconds to let your body relax.
3. Now while inhaling raise your upper body up as shown in above image.
4. Place your chin in your palms and keep breathing deeply.
5. Hold this position for few minutes.
6. Now while exhaling release your pose. Remove your palms and bring down your shoulders and chin on the ground.
7. Repeat this for few more times.

Benefits

- It is an excellent yoga exercise for relieving back pain.
- Effective to reduce stress, anxiety, and depression.
- Improves blood circulation.
- Much effective to prevent constipation and indigestion.
- Beneficial in the treatment of high blood pressure and heart disease.
- Stretches your spine and brings flexibility.

Precautions

- Those who are suffering from serious back pain, neck and beck injuries should not practice.
- Always practice under an expert guidance if you are suffering from any health issues.

4.MATERIALS AND METHODS

4.1.METHODOLOGY :

STUDY TYPE : A preclinical and clinical study.

STUDY DESIGN

Study Place : OPD and IPD of Ayothidoss Pandithar Hospital, National Institute of Siddha, Tambaram Sanatorium, Chennai - 47.

Study Period : 18 Months

Year : 2016-2019.

Sample Size : 40 patients (20 Patients in OPD and 20 Patients in IPD)

4.2.TRAIL DRUG :

Internal Medicine : *Parangipattai kudineer (PPK)*[35]

Dosage : 30 ml , Three times a day (Before food)

Duration of Treatment : 4 8 days

Reference : Pharmacopoeia of hospital of Indian medicine

Page .No : 3

Edition : 2nd edition 1995

Edited & Publish by : Directorate of Indian medicine & Homeopathy.

External Medicine : **Sivappu Thylam**[36]

Reference : Pharmacopoeia of hospital of Indian medicine

Page.No : 33

Edition : 2nd edition 1995

Dosage : Required quantity **(**Local application**)**

Edited & Publish by : Directorate of Indian medicine & Homeopathy.

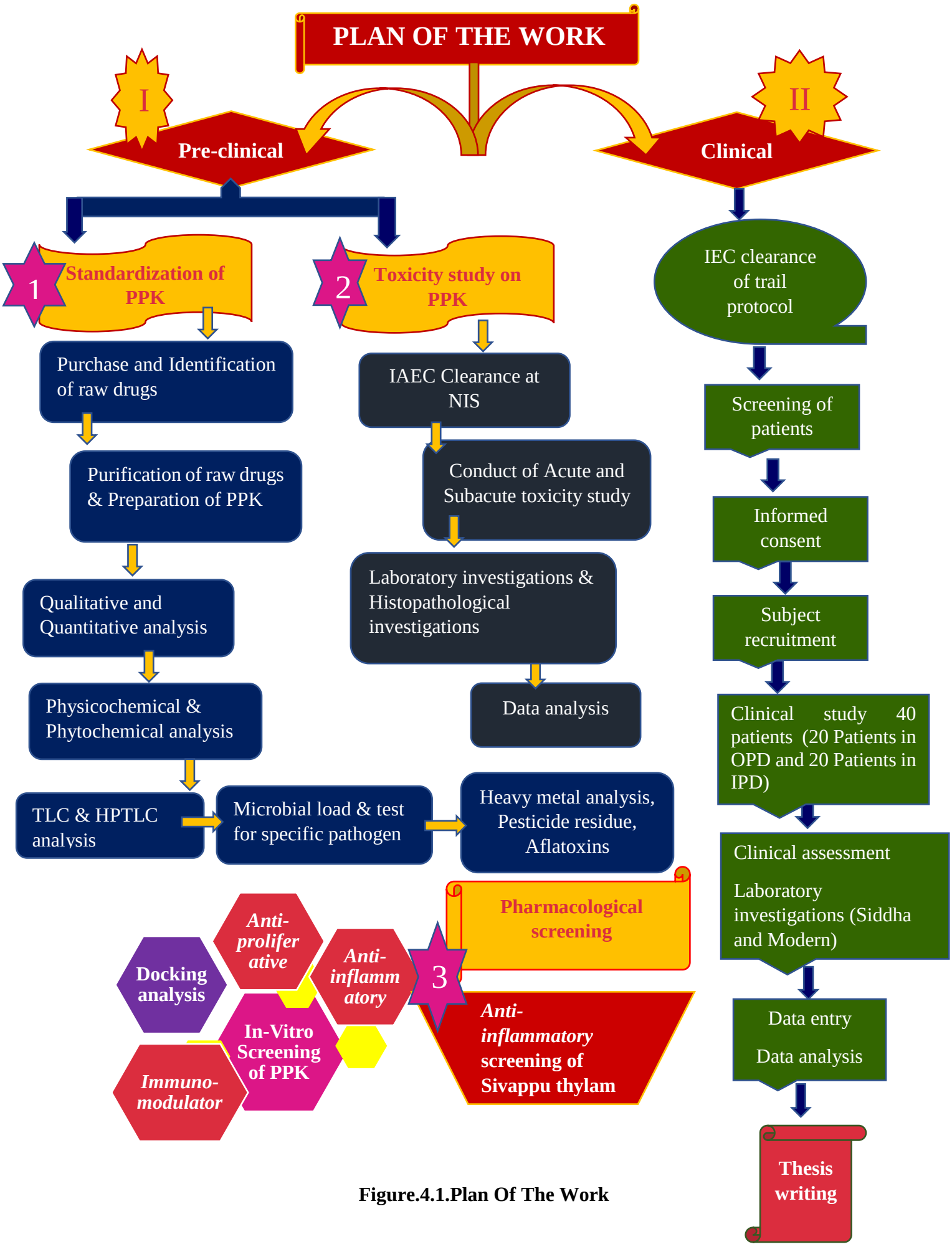


Figure.4.1.Plan Of The Work

4.3..Standard Operating Procedure:

Source of raw drugs:

The required raw drugs for the trial medicine purchased from a well reputed country raw drug shop and drugs was authenticate by the competent authority Medicinal Botany and CCRS. After that the raw drugs was purified separately then the trial drugs prepared in Gunapadam laboratory of National Institute of Siddha.

4.4.1..INTERNAL DRUG: *PARANGIPATTAI KUDINEER*

Ingredients:

1.Parangipattai (Smilax chin. Linn.) ---1.000kg

2.Kadugu Rohini (Picrorhiza kurroa.Royle) ---1.000kg

3.Manjitti (Rubia cordifolia.Linn.) ---1.000kg

4.Mara Manjal (Coscinium fenestratum.Colebr.)---1.000kg

5.Kadukkai (Terminalia chebula.Retz.) ---1.000kg

6.Thandrikai (Terminalia bellarica.Roxb) ---1.000kg

7.Vasambu (Acorus calamus.Linn.) ---1.000kg

8.Sombu (Pimpinella anisum.Linn) ---1.000kg

9.Veppampattai (Azadirachta indica.A.Juss) ---1.000kg

10.Seendhil (Tinospora cordifolia.Miers) ---1.000kg

Figure.4.1..Image of ingredients of Parangipattai Kudineer

1. 
2. 
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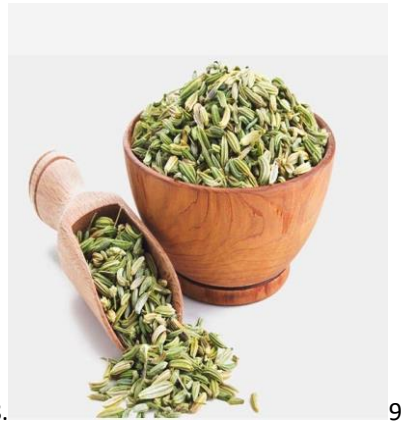
8. 
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1.Smilax china.Linn 2.Picrorhiza kurroa.Royle 3.Rubia cordifolia.Linn

4.Coscinium fenestratum.Colebr 5.Terminalia chebula.Retz 6.Terminalia bellerica.Roxb

7.Acorus calamus.Linn 8.Pimpinella anisum.Linn 9.Azhadirachta indica.A.Juss

10.Tinospora cordifolia.Mier

4.4.2..METHOD OF PURIFICATION OF RAW DRUGS:

1. ***Parangipattai (Smilax china Linn.)***

It should be cleaned with white cloth then the outer layer of parangipattai root bark to be peeled out.(Ref: Sigicharathina theebam:28)

2. ***Kadugu Rohini (Picrorhiza kurroa.Royle.)***

It should be soaked in the neemleaf juice for 3 hours and it should be dried under sunlight.(Ref: Sigicharathina theebam:30)

3. ***Manjitti (Rubia cordifolia.Linn.)***

It should be dried under sunlight.(Ref: Sigicharathina theebam:30)

4. ***Mara Manjal (Coscinium fenestratum.Colebr)***

The outer skin should be removed.(Ref: Sigicharathina theebam:29)

5. ***Kadukkai(Terminalia chebula.Retz)***

The seed removed and rinds alone to be used for preparation.(Ref:Sigicharathina theebam:30)

6. ***Thandrikai(Terminalia bellarica.Roxb)***

The seed removed and rinds alone to be used for preparation.(Ref: Sigicharathina theebam:30)

7. ***Vasambu(Acorus calamus.Linn)***

It should be cleaned with white cloth then the outer layer of vasambu root bark to be peeled out (Ref: Sigicharathina theebam:30)

8. ***Sombu (Foeniculum vulgare.Linn)***

It should be dried for six hours under sunlight. (Ref: Sigicharathina theebam:29)

9. ***Veppampattai(Azadirachta indica .A.Juss.)***

It should be cleaned with white cloth then the outer layer of veppampattai's bark to be peeled out.(Ref: Sigicharathina theebam:28)

10. ***Seendhil(Tinospora cordifolia .Miers.)***

The outer skin of stem should be removed. (Ref: Sigicharathina theebam:33).

4.4.3.METHOD OF PREPARATION:

All the drugs was purified and crushed into coarse powder. Then adding 8 times of water with the coarse powder before boiling. Preparing the decoction by reduced it into 1/8.

Figure.4.2..Image of Pepared PPK

4.4.4.Dosage **: 30ml , Three times a day (Before food).**

4.4.5...Route of administration : Per oral

4.4.6...Duration of Treatment : 48 days.

4.4.7..Indications **: All skin diseases, insect bites etc.**

4.5.EXTERNAL MEDICINE: SIVAPPU THYLAM

4.5.1.Ingredients of Sivappu thylam :

1. Pungan Ver (Pongamia pinnata Pierre.) -- 4kg

2. Manjitti (Rubia cordifolia Linn.) -- 62.5gm

3. Nannari (Hemidesmus indicus R.Br.) -- 62.5gm

4. Manjal Mezhugu (Cera wax) -- 62.5gm

5. Vellai Kungiliyam (Vateria indica Linn.) -- 62.5gm

6. Chevvallikkodi (Dioscorea purpurea) -- 20gm

7. Surul Pattai (Cinnamomum verum.Juss.) -- 30gm

8. Coconut Oil (Cocos nucifera Linn.) -- 1 Lr

Figure.4.3..Image of Ingredients of Sivappu thylam :

4.5.2.METHOD OF PREPARATION :

The Manjitti, Nannari, Chevvallikodi, PunganVer and adding 8 times of water then boiled. Prepare the decoction by reduced it into 1/8.Then equal quantity of oil should be mixed with the decoction and again to be boil.The yellow wax should be cut into pieces and added them into the melted thick consistency. After melting, it will be taken from the oven in the texture of sand. Then the pulverized Surulpattai (lavangapattai) added into it and stirr well.Then filter and keep it for use.

Figure.4.4.Image of Pepared Sivappu thylam

4.5.3.Dosage **:** Required quantity **(**Local application**)**

4.5.4.Duration of Treatment : 48 days.

4.5.5.Indications **: All skin diseases.**

4.5.6.Drug Storage:

The trial drug ***Parangipattai Kudineer powder*** is stored in clean and dry container. ***Sivappu Thylam*** is stored in clean and dry narrow mouthed bottles.

4.6.Dispensing:

The *Parangipattai Kudineer powder 10gram/time* is given in packets and *Sivappu Thylam* quantity sufficient is given in bottles.

4.7.ANALYTICAL SPECIFICATION FOR CHOORANAM

4.7a.PHYSIOCHEMICAL ANALYSIS[41,42] :

4.7a.1.Loss On Drying:

An accurately weighed 2g of parangipattai kudineer chooranam formulation was taken in a tarred glass bottle. The crude drug was heated at 105^0 C for 6 hours in an oven till a constant weight. The percentage moisture content of the sample was calculated with reference to the shade dried material.

4.7a.2. Determination of total ash:

Weighed accurately 2g of parangipattai kudineer chooranam formulation was added in crucible at a temperature 600^0 C in a muffle furnace till carbon free ash was obtained. It was calculated with reference to the air dried drug.

4.7a.3. Determination of acid insoluble ash:

Ash above obtained, was boiled for 5 min with 25ml of 1 M hydrochloride and filtered using an ash less filter paper. Insoluble matter retained on filter paper was washed with hot water and filter paper was burnt to a constant weight in a muffle furnace. The percentage of acid insoluble as was calculated with reference to the air dried drug.

4.7a.4. Determination of water soluble ash:

Total ash 1g was boiled for 5min with 25ml water and insoluble matter collected on an ash less filter paper was washed with hot water and ignited for 15min at a temperature not exceeding 450^0 C in amuffle furnace. The amount of soluble ash is determined by drying the filtrate.

4.7a.5. Determination of water soluble extractive:

5gm of air dried drug, coarsely powered parangipattai kudineer chooranam was macerated with 100ml of distilled water in a closed flask for twenty-four hours, shaking frequently. Solution was filtered and 25ml of filtered and 25ml of filtrated was evaporated in a tarred flat bottom shallow dish, further dried at 100^0 C and weighted. The percentage of water soluble extractive was calculated with references to the sir dried drugs.

4.7a.6. Determination of alcohol soluble extractive:

2.5gm of air dried drugs, coarsely powdered parangipattai kudineer chooranam was macerated with50ml. The alcohol in closed flak for 24 hrs. With frequent shaking, it was filtered rapidly taking precaution against loss of alcohol. 10ml of filtrate was then evaporated in a tarred flat bottom shallow dish, dried at 100^0 C and weighted. The percentage of alcohol soluble extractive was calculated with reference to air dried drug.

4.7a.7.Determination of pH

About 5 g of test sample will be dissolved in 25ml of distilled water and filtered the resultant solution is allowed to stand for 30 mins and the subjected to pH evaluation

4.7a.8.Particle Size Determination [37,38] :

Particle Size for the Test Sample- PKC determined by Electron Microscopic Observation.

4.7a.9.Microbiological contaminant study :

Sterility test by pour plate method :

Objective

The pour plate techniques were adopted to determine the sterility of the product. Contaminated / un sterile sample (formulation) when come in contact with the nutrition rich medium it promotes the growth of the organism and after stipulated period of incubation the growth of the organism was identified by characteristic pattern of colonies. The colonies are referred to as Colony Forming Units (CFUs).

Methodology

Test sample was admixed with sterile distilled water and the mixture were been used for the sterility evaluation. About 1ml of the test sample was inoculated in sterile petri dish to which about 15 mL of molten agar 45^{o}C were added. Agar and sample were mixed thoroughly by tilting and swirling the dish. Agar was allowed to completely gel without disturbing it. (about 10 minutes). Plates were then inverted and incubated at 37^{o} C for 24-48 hours. Grown colonies of organism was then counted and calculated for CFU.

4.7a.10.TLC & HPTLC analysis of aqueousextract of Parangipattai Kudineer Chooranam (PKC)[39]:

TLC Analysis

Test sample was subjected to thin layer chromatography (TLC) as per conventional one dimensional ascending method using silica gel 60F254, 7X6 cm (Merck) were cut with ordinary household scissors. Plate markings were made with soft pencil. Micro pipette were used to spot the sample for TLC applied sample volume 10-micro liter by using pipette at distance of 1 cm at 5 tracks. In the twin trough chamber with the specified solvent system After the run plates are dried and was observed using visible light Short-wave UV light 254nm and light long-wave UV light 365 nm

High Performance Thin Layer Chromatography Analysis[40]

HPTLC method is a modern sophisticated and automated separation technique derived from TLC. Pre-coated HPTLC graded plates and auto sampler was used to achieve precision, sensitive, significant separation both qualitatively and quantitatively. High performance thin layer chromatography (HPTLC) is a valuable quality assessment tool for the evaluation of botanical materials efficiently and cost effectively. HPTLC method offers high degree of selectivity, sensitivity and rapidity combined with single-step sample preparation. Thus this method can be conveniently adopted for routine quality control analysis. It provides chromatographic fingerprint of phytochemicals which is suitable for confirming the identity and purity of phytotherapeutics.

Chromatogram Development

It was carried out in CAMAG Twin Trough chambers. Sample elution was carried out according to the adsorption capability of the component to be analyzed. After elution, plates were taken out of the chamber and dried.

Scanning

Plates were scanned under UV at 366nm. The data obtained from scanning were brought into integration through CAMAG software. Chromatographic finger print was developed for the detection of phytoconstituents present in each sample and their respective Rf values were tabulated.

7a.1.11.Heavy Metal Analysis by AAS[41,42]

Standard: Hg, As, Pb and Cd – Sigma

Methodology

Atomic Absorption Spectrometry (AAS) is a very common and reliable technique for detecting metals and metalloids in environmental samples. The total heavy metal content of the sample was performed by Atomic Absorption Spectrometry (AAS) Model AA 240 Series. In order to determination the heavy metals such as mercury, arsenic, lead and cadmium concentrations in the testitem.

Sample Digestion

Test sample was digested with 1mol/L HCl for determination of arsenic and mercury. Similarly for the determination of lead and cadmium the sample were digested with 1mol/L of HNO3.

Standard reparation

As & Hg- 100 ppm sample in 1mol/L HCl Cd & Pb- 100 ppm sample in 1mol/L HNO_3

4.7a.11..Pesiticide Residue[41,42] :

Extraction

Test sample were extracted with 100ml of acetone and followed by homogenization for brief period .Further filtration was allowed and subsequent addition of acetone to the test mixture. Heating of test sample was performed using a rotary evaporator at a temperature not exceeding 40ºC until the solvent has almost completely evaporated. To the residue add a few millimetres of toluene R and heat again until the acetone is completely removed. Resultant residue will be dissolved using toluene and filtered through membrane filter.

4.7a .12.Test for Specific Pathogen[41,42]

Methodology

One part of the test sample was dissolved in 9 mL of sterile distilled water and the test sample was directly inoculated in to the specific pathogen medium (EMB, DCC, Mannitol ,Cetrimide) by pour plate method. The plates were incubated at 37ºC for 24 - 72h for observation. Presence of specific pathogen identified by their characteristic colour with respect to pattern of colony formation in each differential media.

Detail of Specific Medium and their abbreviation

Organism	Abbreviation	Medium
E-coli	***EC***	***EMB Agar***
Salmonella	***SA***	***Deoxycholate agar***
Staphylococcus Aureus	***ST***	***Mannitol salt agar***
Pseudomonas Aeruginosa	***PS***	***Cetrimide Agar***

4.7a.13..Aflatoxin Assay By TLC (B1,B2,G1,G2)[43] :

Standard :
Aflatoxin B1
Aflatoxin B2
Aflatoxin G1
Aflatoxin G2

Solvent

Standard samples was dissolved in a mixture of chloroform and acetonitrile (9.8 : 0.2) to obtain a solution having concentrations of 0.5 µg per ml each of aflatoxin B1 and aflatoxin G1 and 0.1 µg per ml each of aflatoxin B2 and aflatoxin G2.

Test solution: Concentration 1 µg per ml

Procedure

Standard aflatoxin was applied on to the surface to pre coated TLC plate in the volume of 2.5 µL, 5µL, 7.5 µL and 10 µL. Similarly the test sample was placed and Allow the spots to dry and develop the chromatogram in an unsaturated chamber containing a solvent system consisting of a mixture of chloroform, acetone and isopropyl alcohol (85 : 10 : 5) until the solvent front has moved not less than 15 cm from the origin. Remove the plate from the developing chamber, mark the solvent from and allow the plate to air-dry. Locate the spots on the plate by examination under UV light at 365nm.

4.7b.Chemical Method Of Testing:

4.7b.1. Phytochemical Analysis:

The following preliminary phytochemical investigations of extract were performed by the standard methods (Harborne, 1973; Markham, 1982; Kokate, 1994).

PRELIMINARY PHYTOCHEMICAL SCREENING -PPK

The preliminary photochemical screening test was carried out for each extracts of parangipattai kudineer chooranam as per the standard procedure.

4.7b.1.1. Detection of alkaloids:

Extracts were dissolved individually in dilute hydrochloride acid and filtered

a) **Mayer's test:** Filter's were treated with Mayer's reagent (potassium mercuric iodide). Formation of a yellow coloured precipitate indicates the presence of alkaloids.
b) **Wager's test:** Filter's were treated with wager's reagent (Iodine in Potassium Iodine). Formation of brown/reddish precipitate indicates the presence of alkaloids.
c) **Dragendroff's test:** Filter's were treated with Dragendroff's reagent (solution of Potassium Bismuth Iodide). Formation of red precipitate indicates the presence of alkaloids.

d) **Hager's test:** Filter's were treated with Hager's reagent (saturated picric acid solution). Presence of alkaloids confirmed by the formation of yellow colored precipitate.

4.7b.1.2. Detection of carbohydrates:

Extracts were dissolved individually in 5 ml distilled water and filtered. The filtrates were used to test for the presence of carbohydrates.

a) Molisch's test:

To 2 ml of plant sample extract, two drops of alcoholic solution of - naphthol are added. The mixture is shaken well and a few drops of concentrated sulphuric acid is added slowly along the sided of test tube. A violet ring indicates the presence of carbohydrates.

b) Benedict's test:

Filtrates were treated with Benedict's reagent and the heated gently. Orange red precipitate indicates the presence of reducing sugars.

4.7b.1.3. Detection of glycoside:

Extract were hydrolyzed with dil.HCL, and then subjected to test for glycoside.

a) Modified borntrager's test: Extract were treated with ferric chloride solution and immersed in boiling water for about 5 minutes . The mixture was cooled and extracted with equal volumes of benzene. The benzene layer was separated and treated with ammonia solution. Formation of rose-pink color in the ammonical layer indicates the presence of anthranol glycosides.

b) Cardiac glycoside (keller -killiani test): Extract was shaken with distilled water (5 ml), To this , glacial acetic acid (2ml) containing a few drops of ferric chloride was added, followed by H2SO4 (1 ml) along the side of the test tube. The formation of brown ring at the interface gives indication for cardiac glycoside and a violet ring may appear below the brown ring.

4.7b.1.4. Detection of saponins:

a) Froth test: Extracts were diluted with distilled water to 20ml and this was shaken in a graduated cylinder for 15 minutes. Formation of 1 cm layer of foam indicates the presence of saponins.

b) Foam test: 0.5gm of extract was shaken with 2ml of water. If foam produced persists for ten minutes it indicates the presence of saponins.

4.7b.1.5.Detection of phytosterols:

a) **Salkowski.s test:** Extract were treated with chloroform and filtered. The filtrates were treated with few drops of conc. sulphuric acid, shaken and allowed to stand. Appearance of golden yellow colour indicates the presence of triterpenes.

4.7b.1.6. Detection of phenols ferric chloride test:

Extracts were treated with 3-4 drops of ferric chloride solution. Formation of bluish black colour indicates the presence of phenols.

4.7b.1.7. Detection of tannins gelatin test:

The extract is dissolved in 5 ml of distilled water and 2 ml of 1% soluti0on of gelatine containing 10% Nacl is added to it. White precipitate indicates the presence of phenolic compounds.

4.7b.1.8. Detection of Flavanoids:

a) Alkaline reagent test: Extracts were treated with few drops of sodium hydroxide solution. Formation of intense yellow color, which becomes colourless on addition of dilute acid, indicates the presence of flavanoids.

b) Lead acetate test: Extract were treated with few drops of lead acetate solution of yellow color precipitate indicates the presence of flavanoids.

4.7b.1.9. Detection of proteins and amino acid:

a) Xanthoproteic test: The extracts were treated with few drops of conc. Nitric acid. Formation of yellow color indicates the presence of proteins.

b) Ninhydrin test: To the extract, 0.25% w/v ninhydrin reagent was added and boiled for few minutes. Formation of blue colour indicates the presence of amino acids.

4.7b.1.10. Detection of diterpenes copper acetate test:

Extracts were dissolved in water and treated with 3-4 drops of copper acetate solution. Formation of emerald green color indicated the presence of diterpenes.

4.7b.1.11. Gum and Mucilage:

To 1 ml of extract add 2.5ml of absolute alcohol and stirring constantly. Then the precipitate was dried in air and examine for its swelling properties. Swelling was observed that will indicates presence of gum and mucilage.

4.7b.1.12. Test for fixed oils and fats:

a) Spot test: A small quantity of extract is pressed between two filter paper. Oil stain on the paper indicates the presence of fixed oils.

4.7b.1.13. Test for quinones:

Extract was treated with sodium hydroxide blue or red precipitate indicates the presence of quinines.

The preliminary phytochemical studies of aqueous extract of parangipattai kudineer chooranam were done using standard procedures.

4.7b.2.CHEMICAL ANALYSIS :

S.No	EXPERIMENT	OBSERVATION
1.	Appearance of sample	Dark brown in colour
2.	**Test for Silicate:** a. A little (500mg) of the sample is shaken well with distilledwater. b. A little(500mg) of the sampleis shaken well with con. HCl/Con. H_2So_4	Insoluble
3.	**Action of Heat:** A small amount (500mg) of the sample is taken in a dry test tube and heated gently at first and then strong.	White fumes evolved No Brown fumes
4.	**Ash Test:** A filter paper is soaked in a mixture of sample and dil. cobalt nitrate solution and introduced into the Bunsen flame and ignited.	No Yellow colour flame appeared

Test For Acid Radicals

S.No	EXPERIMENT	OBSERVATION
1.	**Test For Sulphate:** 2ml of the above-prepared extract was taken in a test tube and 2ml of 4% dil. ammonium oxalate solution was added.	No Cloudy appearance
2.	**Test For Chloride:** 2ml of the above-prepared extracts was added with 2ml of dil-HNO_3 until the effervescence ceases off. Then 2 ml of silver nitrate solution was added.	Presence of Cloudy appearance
3.	**Test For Phosphate:** 2ml of the extract was treated with 2ml of con.HNo3 and 2ml of dil. ammonium molybdate solution.	Cloudy Yellow appearance present
4.	**Test For Carbonate:** 2ml of the extract was treated with 2mldil. magnesium sulfate solution	Presence of Cloudy appearance
5.	**Test For Sulphide:** 1gm of the substance was treated with 2ml of the con.HCL	Rotten Egg Smelling gas was not evolved
6.	**Test For Fluoride & Oxalate:** 2ml of the extract was added with 2ml of dil. Acetic acid and 2ml dil. calcium chloride solution and heated.	No Cloudy appearance
7.	**Test For Nitrite:** 3drops of the extract was placed on a filter paper, on that-2 drops of dil. acetic acid and 2 drops of dil. Benzidine solution was placed.	Characteristic changes not appeared
8.	**Test for Borate:** 2 pinches of the substance is made into paste by using sulphuric acid and alcohol (95%) and introduced into the blue flame	Bluish green colour flame not appeared

1.	**Test For Lead:** 2ml of the extract was added with 2ml of dil. potassium iodinesolution.	Yellow Precipitate was not obtained.
2.	**Test For Copper:** One pinch (50mg) of substance was made into a paste with con. HCl in a watch glass and introduced into the non- luminous part of theflame.	The blue colour precipitate formed.
3.	**Test For Aluminium:** In the 2ml of extract dil. sodium hydroxide was added in 5 drops toexcess.	Yellow colour was not formed

Test For Basic Radicals

4.	**Test For Iron:** a. To the 2ml of extract add 2ml of dil. ammoniumsolution b. To the 2ml of extract, 2ml thiocyanate solution and 2ml of con HNo3 isadded	Absence of brown precipitate Red colour formed
5.	**Test For Zinc:** In 2ml of the extract dil. sodium hydroxide solution was added in 5 drops to excess and dil. Ammonium chloride wasadded.	White precipitate was not formed
6.	**Test For Calcium:** 2ml of the extract was added with 2ml of 4% dil. ammonium oxalate solution	No Cloudy appearance and white preciptitate is obtained

7.	**Test For Ammonium:** In 2ml of extract 1 ml of Nessler's reagent and excess of dil. sodium hydroxide solution was added.	Brown colour not formed
8.	**Test For Potassium:** A pinch (25mg) of substance was treated with 2ml of dil. sodium nitrite solution and then treated with 2ml of dil. cobalt nitrate in 30% dil. glacial acetic acid.	No Yellowish precipitate formed
9	**Test For Sodium:** 2 pinches (50mg) of the substance was made into a paste by using HCl and introduced into the blue flame of Bunsen burner.	Yellow colour flame not appeared
10	**Test For Mercury:** 2ml of the extract was treated with 2ml of dil. sodium hydroxide solution.	Yellow precipitate not formed
11	**Test For Arsenic:** 2ml of the extract was treated with 2ml of dil. sodium hydroxidesolution.	Brownish red precipitate not formed

Other constituents

1.	**Test For Starch:** 2ml of extract was treated with weak dil. iodine solution	No Blue colour developed
2.	**Test For Reducing Sugar:** 5ml of Benedict's qualitative solution was taken in a test tube and allowed to boil for 2minutesandadded8to10dropsofthe extract and again boil it for 2 minutes.	The was no specific change in colour
3.	**Test For The Alkaloids**: a) 2ml of the extract is treated with 2ml of dil. Potassium iodide solution. b) 2ml of the extract is treated with 2ml of dil. picricacid.	Reddish brown precipitation not formed Yellow precipitation formed
4.	**Test For Tannic Acid:** 2ml of the extract was treated with 2ml of dil. ferric chloride solution	Black precipitate not formed
5.	**Test For Amino Acid:** 2 drops of the extract were placed on a filter paper and dried well, and then 20ml of Biuret reagent was added to it.	Violet colour not developed
6.	**Test for Type of Compound:** 2 ml of the extract is treated with 2 ml of ferric chloride solution	No Green color developed

4.7c.PHARMACOLOGICAL SCREENING OF PARANGIPATTAI KUDINEER CHOORANAM :

4.7c.1.In-vitro Anti-Inflammatory Activity by Protein (Albumin) denaturation Assay[44,45]

Albumin Denaturation Assay Procedure

In-vitro anti-inflammatory activity PKC was studied using albumin denaturation technique. The reaction mixture consisted of bovine serum albumin (5% aqueous solution) and test sample PKC at varying concentration ranges from 100 to 500 µg/ml and standard Diclofenac sodium at the concentration of 100 µg /ml of final volume. pH was adjusted by using a small amount of 1N Hydrochloric acid. The samples were incubated at 37°C for 20 min and then heated at 57°C for 3 min. After cooling the sample, 2.5 ml of phosphate buffer solution was added into each test tube. Turbidity developed was measured spectrophotometrically at 660 nm, for control distilled water was used instead of test sample while product control tests lacked bovine serum albumin. The experiment was performed in triplicate.

The Percentage protection from denaturation is calculated by using the formulae

$$\left[\frac{(A)_{\text{control}} - (A)_{\text{sample}}}{(A)_{\text{control}}}\right] \times 100.$$

4.7c.2.In vitro Immunomodulatory Activity of Siddha formulation *Parangipattai Kudineer Chooranam* (PKC) in RAW Macrophage Cell line[46,47] :

Immunomodulatory activity Materials and Methods

For anti-proliferative studies, serial dilutions of test formulation (50, 100 and 200 µg/ml) were prepared.

Culture: Macrophage cell line RAW 264.7

Cell culture, measurement of cell viability

Macrophage cell line RAW 264.7 was obtained from National Center for Cell Science (Pune, India) and cultured in DMEM supplemented with fetal bovine serum (10%) containing penicillin-streptomycin (10%) at 37°C in a humidified atmosphere containing 5% CO2. Cells were plated at a density of 1 × 104 cells/well in 25 or 75 cm2 flasks, or in 96-well plate overnight. RAW 264.7 were grown to 60% confluence followed by activation with 1 µL lipopolysaccharide (LPS) (1µg/mL). LPS stimulated RAW cells were exposed with different

concentration (50, 100,200 µg/mL) of the test sample and incubated for 24 hours. After 24 hours of incubation, the cells were digested and centrifugation was done at 6000 rpm for 10 minutes. Supernatant was discarded and cells were then resuspended in 200µl of cell lysis buffer (0.1M TrisHCl, 0.25M EDTA, 2M NaCl, 0.5 % Triton x-100). The samples were then kept at 4^{o}C for 20 minutes. After incubation, the Immunomodulatory response was performed by estimating nitrite levels in the cell lysate.

Estimation of Cellular Nitrite Levels

The level of nitrite level was estimated by the method of Lee et al. (Lepoivre et. al. 1990) To 0.5 mL of cell lysate, 0.1 mL of sulphosalicylic acid was added and vortexed well for 30 minutes. The samples were then centrifuged at 5,000 rpm for 15 minutes. The protein-free supernatant was used for the estimation of nitrite levels. To 200 µL of the supernatant, 30 µL of 10% NaOH was added, followed by 300 µL of Tris-HCl buffer and mixed well. To this, 530 µL of Griess reagent was added and incubated in the dark for 10–15 minutes, and the absorbance was read at 540 nm against a Griess reagent blank. Sodium nitrite solution was used as the standard. The amount of nitrite present in the samples was estimated from the standard curves obtained.

4.7c.3.In vitro Anti-proliferative Activity of Siddha formulation *Parangipattai Kudineer Chooranam* (PKC) in HaCaT cell line using MTT assay[48,49] :

Anti-proliferative activity

The *In Vitro* determinations of anti-proliferative effects of the test formulation have been performed by counting viable cells after staining with a vital dye. The MTT system is a means of measuring the activity of living cells via mitochondrial dehydrogenases. The MTT method is simple, accurate and yields reproducible results. The key component is (3-[4, 5-dimethylthiazol-2-yl]-2, 5-diphenyl tetrazolium bromide) or MTT, is a water soluble tetrazolium salt upon incubation MTT is converted to an insoluble purple formazan by cleavage of the tetrazolium ring by mitochondrial dehydrogenase enzymes of viable cells. The resulting colored solution is spectrophotometrically measured. An increase or decrease in cell number results in a concomitant change in the amount of formazan formed, indicating the degree of cytotoxicity caused by the test material.

Preparation of test solutions

For anti-proliferative studies, serial dilutions of test formulation (10, 50, 100, 150, 200 and 250 µg/ml) were prepared.

HaCat Cell culture and media

HaCaT cell lines were procured from NCCS, stock cells was cultured in DMEM medium supplemented 0.07 mM Ca2+,10% heat-inactivated fetal bovine serum, glutamine (2 mM), penicillin (100 U⁄ml), and streptomycin (100 mg⁄ml) in an humidified atmosphere of 5% CO_2 at 37°C until confluent. The cell was dissociated with TPVG solution (0.2 % trypsin, 0.02 % EDTA, 0.05 % glucose in PBS). The viability of the cells are checked, centrifuged and was seeded in a 96 well plate and incubated for 24hrs – 7 days at 37°C, 5% CO_2 incubator.

Anti- proliferation assay

For anti- proliferation assay, 1.25 x 10^4 HaCaT cells, were seeded per well in 96-well culture plates and incubated overnight. Growth medium was then substituted with fresh medium supplemented with tested compounds at appropriate concentrations. Following incubation for 24 and 48 hours till 7 -days (to test cell proliferation), medium was substituted with MTT solution and after a 2-hour incubation at 37°C the formazan product was dissolved and absorbance was read at 570 nm using microplate reader. The optical density of formazan formed in the control and test drug treated wells was taken as a measure of cell viability. IC_{50} was calculated from dose-response curves.

$$\text{Survival rate (\%)} = \frac{A_{sample} - A_b}{A_c - A_b} \times 100$$

4.7c.4.Docking analysis [50,51,52,53]:

Objective:

Binding of lead/ drug with these core amino acids by forming hydrogen bond will hinders the functions of TNF-α, IL-6 and Nitric oxide synthase, since these are the core cytokines involved in mediating the immune system. Thereby lead molecules which halts the generation of cytokines may prevents the immune mediated inflammation.

Name of the formulation : Parangipattai Kudineer Chooranam (PKC)

List of herbs present in the formulation

1.Parangi pattai (Simlax Chin Linn)

2.Kadugu Rohini (*Picrorhiza kurroa*)

3.Manjitti (Rubia Cordifolia)

4. Mara Manjal (Coscinium fenestratum)

5.Kadukkai (Terminalia Chebula)

6.Thandrikai (Terminalia Bellarica)

7.Vasambu (Acorus Calamus)

8.Sombu (Pimpinella Anisum)

9.Veppampattai (Azardirachta Indica)

10.Seendhil (Tinospora Cordifolia)

List of Phytocomponents Selected for docking

Herbs	**Phyto components**	**References**
1.Parangi pattai (Simlax Chin Linn)	Protocatechuic acid, Kaempferol	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6155388/
2.Kadugu Rohini (*Picrorhiza kurroa*)	Picein	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3783750/
4.Sombu (Pimpinella Anisum)	Anisaldehyde	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3405664/
5.Veppampattai (Azardirachta Indica)	Nimbolide	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4791507/
6.Seendhil (Tinospora Cordifolia)	Berberine	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3644751/

Methodology

Docking calculations were carried out using Auto Dock 4. Gasteiger partial charges were added to the ligand atoms. Non-polar hydrogen atoms were merged, and rotatable bonds were defined. Docking calculations were carried out for the compounds retrieved such as Anisaldehyde , Berberine, Kaempferol, Protocatechuic acid, Nimbolide, Picein and their respective standard Tacrolimus against target protein model. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of Auto Dock tools (*Morris, Goodsell et al., 1998*). Affinity (grid) maps of ×× Å grid points and 0.375 Å spacing were generated using the Autogrid program (*Morris, Goodsell et al., 1998*). Auto

Dock parameter set- and distance-dependent dielectric functions were used in the calculation of the van der Waals and the electrostatic terms, respectively. Docking stimulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (*Solis and Wets, 1981*). Initial position, orientation, and torsions of the ligand molecules were set randomly. All rotatable torsions were released during docking. Each docking experiment was derived from 2 different runs that were set to terminate after a maximum of 250000 energy evaluations. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied.

4.7d.Sivappu Thylam :

7d.1.In-vitro Anti-Inflammatory Activity by Protein (Albumin) denaturation Assay[54,55]

Albumin Denaturation Assay Procedure

In-vitro anti-inflammatory activity ST was studied using albumin denaturation technique. The reaction mixture consisted of bovine serum albumin (5% aqueous solution) and test sample ST at varying concentration ranges from 100 to 500 µg/ml and standard Diclofenac sodium at the concentration of100 µg /ml of final volume. pH was adjusted by using a small amount of 1N Hydrochloric acid. The samples were incubated at 37°C for 20 min and then heated at 57°C for 3 min. After cooling the sample, 2.5 ml of phosphate buffer solution was added into each test tube. Turbidity developed was measured spectrophotometrically at 660 nm, for control distilled water was used instead of test sample while product control tests lacked bovine serum albumin. The experiment was performed in triplicate.

The Percentage protection from denaturation is calculated by using the formulae

$$\left[\frac{(A)_{\text{control}} - (A)_{\text{sample}}}{(A)_{\text{control}}}\right] \times 100.$$

4.e.SAFETY STUDIES[56]:

The acute and subacute toxicity studies on animals were conducted at animal house, National Institute of Siddha (Reg.no : 1248/GO/RE/2009/CPCSEA),Chennai-47. (**IAEC NO:NIS / IAEC VI / 2404 / 2018 /09)**.

ACUTE AND SUBACUTE TOXICITY STUDY :

Objective :

The "Acute oral Toxicity Study of "**Parangipattai Kudineer"** on Wistar albino rats was to evaluated the toxicological studies of the drug as per guideline and IAEC guidance.

Test Guideline Followed:

Acute toxicity study was conducted as per OECD- 423 Guideline with slight modification.

4.e.1.ACUTE TOXICITY STUDY :

4.e.1.1.Materials and Methods:

The acute toxicity study was conducted on 8-12 weeks old Albino rats of female sex weighing 140-160g . These animals were selected because literature surveys of conventional LD50 tests show that, although there is little difference in sensitivity between the sexes, in those cases where differences are observed females are generally slightly more sensitive .The body weight range should be within ± 20% of the mean body weight at the time of Randomization and grouping for acute and subacute toxicity study.The rats were purchased from The Tamilnadu Veterinary and animal sciences university, Madhavaram milk colony ,Chennai and housed in standard laboratory condition in Polypropylene cages, provided with Rodent pelleted feed,Ro purified water *ad libitum.*

4.e.1.2.Acclimatization:

The animals were selected after veterinary examination by the veterinarian; selected rats were kept under acclimatization for a week.

4.e.1.3.Randomization & grouping:

After acclimatization, Rats were randomized as control and PPK treated group as followed,

Acute toxicity study-14 days (OECD Guidelines - 423)

Groups	No. of Rat
Group I : Test drug (***PPK***)-2000mg/kg b.wt	6F (3F+3F)

***PPK-Parangipattai Kudineer**

PPK has not vehicle so single group only conducted without control group by IAEC guidance.

4.e.1.4.Identification:

Animals were housed with appropriate identification by colouring the fur with picric acid solution prepared in water and with cage cards.

4.e .1.5.Husbandry:

Housingand Environmental conditions:

Animals were housed in 1 groups (2/cage) in polypropylene cages in a well ventilated room under a temperature of 22 ± 3°C and 30 - 70% relative humidity, with a 12-hr light/dark artificial light cycle. .Paddy husk was used as bedding. Each cage contained a maximum of 3 rats. The cages corresponding to each experimental group were distributed on racks in such a manner that outside factors, such as environmental conditions, were balanced as far as possible.

Feed & feeding schedule:

Feed was provided from 'National institute of Siddha animal house, Chennai. The animals had free access.

Water:

The water was offered ad libitum in bottles. This was periodically analysed to detect the presence of possible contaminants.

4.e.1.6.Doses:

Following the fasting period, the animals were weighed and then PPK was administered orally as single dose using a needle fitted onto a disposable syringe of approximate size.

The drug was administered at 2gms/kg b.wt as a single dose. After administration period, all animals were observed for 14 days.

4.e .1.7.Administration:

The test item was administered orally to each female Wister rats as single dose using a needle fitted onto a disposable syringe of appropriate size.

4.e.1.8.Observation period:

After drug administration observations were started to be recorded at the ½ hr, 1hour, 2hours, 4hours on day one of dosing and twice daily after that for the next 13 consecutive days. At the 14th day, sensory reactivity to stimuli of different types was conducted. Auditory stimuli responses were measured by clicker sound from approximately 30 cm to the rats; visual stimuli response were measured with the help of shining pen light in the eye of rats and placing a blunt object near to the eye of rats. Response to proprioceptive stimuli was measured by placing anterior/dorsal surface of animals paw to the table edge. The responses of reactions for these three exercises were normal in animals belonging to both the controls as well as drug treatment

dose groups. On day 15, the overnight fasted animals (water allowed *ad libitum*) were sacrificed and examine for gross pathological changes in the major internal organs.

4.e.1.9.Body Weight:

Individual weights of animals were determined before PPK administration, weekly thereafter and at 14 days.

4.e.1.10.Food Consumption:

The quantity of feed was accessible based on the requirement to the group of animal housed in each cage (3 rats). The leftover of the feed was calculated weekly once. The feed consumed /3 animals /cage /week were calculated by subtraction of left over from total quantity of feed offered during that week.

4.e.1.11.Sacrifice and macroscopic examination:

At the end of study period, the overnight fasted (water *ad libitum*) animals were anaesthetized with ketamine, the animals in control and PPK treated group were sacrificed on 15^{th} day and gross pathological changes were observed in the experimental animals.

Statistical analysis:

Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by Dunnett's. $P< 0.05$ considered as significant by comparing treated group with control group using Graph Pad Prism 4.0.

4.e.2.SUBACUTE TOXICITY STUDY:

4.e.2.1.Objective:

Sub Acute toxicity study was conducted as per OECD-407Guideline. Animals should be observed for 28 days during the PPK administration. Sub acute study give information on the health hazard likely to arise from frequent exposure over a relatively period of 28 days.

4.e.2.2.Test Guideline Followed

OECD 407 Method - Sub-Acute Toxic Class Method (Repeated Dose 28-Day Oral Toxicity Study in Rats).

4.e.2.3.Good Laboratory Practices

The study was conducted following the principles of good Laboratory Practice as set for the Principles of Good Laboratory Practice, OECD, 1998.

4.e .2.4. Staff safety

Personnel handling the test item were worn appropriate shielding clothing to avoid inhalation, Skin contact with the test item.

4.e.2.5.Materials and methods

Detail of subacute test :

Young adult Wister albino rats of 8-12 weeks old weighing 140-160 gms of both the sex was used for this study. The body weight range should be within ± 20% of the mean body weight at the time of Randomization and grouping. Animals were housed in four groups (4/cage/sex) in polypropylene cages in a well ventilated room under a temperature of 22 ± 3°C and 30 - 70% relative humidity, with a 12-hr light/dark artificial light cycle. The rats were purchased from The Tamilnadu Veterinary and animal sciences university, Madhavaram milk colony ,Chennai and housed in standard laboratory condition in Polypropylene cages, provided with Rodent pelleted feed,Ro purified water *ad libitum*..

4.e 2.6.Acclimatization

The animals were selected after veterinary examination by the veterinarian. All the selected animals were kept under acclimatization for a week.

4.e.2.7.Randomization & grouping:

One day before the initiation of treatment (last day of acclimatization), the selected animals were randomly grouped into four different groups containing 5 male animals and 5 female animals per group.

4.e .2.8.Numbering and Identification:

Animals were housed with appropriate identification by colouring the fur with picric acid solution prepared in water and with cage cards.

The group no., cage no., sex of the animal and animal no. were identified as indicated below using cage label and body marking on the animals:

Table.4.e.1. Numbering and Identification of animals in subacute toxicity study

Cage No	Group No	Animal Marking	Sex
1	ICONTROL Male	H,B,T,HB,BT	Male
2	ICONTROL Female	H,B,T,HB,BT	Female
3	IILOW DOSE Male	H,B,T,HB,BT	Male
4	IILOW DOSE Female	H,B,T,HB,BT	Female
5	IIIMID DOSE Male	H,B,T,HB,BT	Male
6	IIIMID DOSE Female	H,B,T,HB,BT	Female
7	IVHIGH DOSE Male	H,B,T,HB,BT	Male
8	III HIGH DOSE Female	H,B,T,HB,BT	Female

4.e.2.9.Husbandry

Housing:

The Wister albino rats were housed in standard polypropylene cages with stainless steel top grill. Paddy husk was used for bedding. The paddy husk was changed at least two times in a week.

Environmental conditions:

The animals were kept in a fresh environment with 12 hr light and 12 hr dark cycles. The air was conditioned at 22 ± 3^0C and the relative humidity was maintained between 30-70% with exhaust facility. The cages corresponding to each experimental group were kept on racks in such a manner that outside factors, such as environmental conditions, were balanced as far as possible.

Feed & feeding schedule:

Feed was provided from 'National institute of Siddha animal house, Chennai. The animals had free accessto feed of standard composition containing all macro and micro nutrients.

Water:

The water was offered *adlibitum* in bottles. There was analysed at regular intervals to detect the presence of possible contaminants.

4.e.2.10.Doses:

The doses for the study were selected based on acute toxicity study. Following the period of fasting, the animals were weighed and then test drug was administered orally as single dose using a needle fitted on to a disposable syringe of approximate size at the following different doses.

Table . 4.e.2. Dose level in subacute toxicity study

Test Group	Dose To Animals (mg/kg body-weight/day)	Number of Animals
Group-1	Control (Distilled Water). 10 ml/kg bw	10 (5male and 5 female)
Group-II	Low dose of PPK 9mg/kg.	10 (5male and 5 female)
Group-III	Mid dose of PPK 18mg/kg	10 (5male and 5 female)
Group-IV	High dose of PPK 36mg/kg.	10 (5 male and 5 female)

***1x=9ml**
Kudineer will be condensed to 2ml

The test item was administered for a period of 28 days. All animals in group I to IV were observed for 28 days.

4.e.2.11.Administration:

The test item was administered orally to each rat as single dose using a needle fitted onto a disposable syringe of appropriate size at the following different doses. The concentration was adjusted according to its body weight; the volume not exceeding 10 ml/kg body weight. Variability in test volume was minimized by adjusting the concentration to make sure a constant volume at all dose levels.

4.e .2.12.Observations:

The observations included but were not restricted to changes in skin and the eyes and mucous membranes and in the respiratory, circulatory, central and autonomous nervous systems and behaviour.

8.2.13.Clinical signs of toxicity:

All the rats were observed at least two times daily with the purpose of recording any symptoms of ill- health or behavioural changes and clinical signs of toxicity daily for 28 days for animals in group I to IV.

4.e.2.14.Food intake:

A measured amount of feed was kept in the cages and then after 24 hrs the left out amount of feed was measured to calculate the amount of food consumed by the rats.

4.e.2.15.Water intake:

Water intake was observed by visual observation during the Study. In addition, the water consumption in each cage was observed daily for a period of 28 days.

4.e.2.16.Bodyweight:

The body weight of rats were recorded one week before the start of treatment, and during the course of the treatment on day one, 7^{th}, 14^{th}, 21^{st} and 28^{th} days (day of sacrifice). The mean weights for all groups and sexes were calculated from the individual weights.

4.e.2.17.Pre-terminal deaths:

All rats were observed twice daily for any pre terminal deaths.

4.e.2.18.Blood Collection:

Blood was collected through abdominal aorta from all the animals of four groups on 28th day. The blood was collected in tubes containing as an anticoagulant (Heparin/EDTA). Animals were fasted over night prior to the blood collection.

4.e.2.19.Laboratory studies:

During the 4th week of treatment, blood were withdrawn from abdominal aorta of animals from each group, under ketamine anaesthesia .The blood samples are used to evaluate Haematological parameters like RBC, WBC, and platelets etc….. The collected blood samples also centrifuged 10000 rpm in 10 minutes to separate the serum. The separated serum used to evaluate biochemical parameters like SGOT, SGPT, ALP and BILIRUBIN etc……...

Hematology

The following hematological parameters were analysed (Autoanalyzer)

Hb : Hemoglobin (g %)

PCV : Packed Cell Volume

WBC : White Blood Corpuscles ($x10^3$/cmm)

RBC : Red Blood Corpuscles ($x10^6$/cmm)

Blood Platelet count ($x10^3$/cmm)

Differential WBC count:

Clinical Biochemistry:

The following clinical Bio parameters were analyzed using Auto analyzer

Total serum protein (g/dl)

ALT/SGPT	:	Alanine amino transferase (U/L)
AST/SGOT	:	Aspartate amino transferase (U/L)
ALP	:	Alkaline serum phosphatase (U/L)
CHL	:	Cholesterol (mg/dL)
TG	:	Triglyceride

4.e.2.20.Sacrifice and macroscopic examination

At the end of study period, the overnight fasted (water *ad libitum*) animals were anaesthetized with ketamine, blood samples were collected from abdominal aorta. After blood collection, the animals in group 1 to 4 were sacrificed on 29^{th} day.

4.e.2.21.Organ weights:

After the macroscopic examination the following organs were weighed after separating the superficial fat: Brain, Heart, Spleen Kidneys, sex organs, Liver and Lungs.

4.e.22. Histopathology:

The target organs from control and drug treated animals were preserved in 10 % buffered neutral formalin for histopathological examination.Control and highest dose animals will be initially subjected to histopathological invstigaion. If any abnormality was found in the highest dose group, then the low and mid group will also be examined. All deviations from normal histology were recorded and compared with corresponding controls.

Statistical analysis:

Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by Dunnett's. $P< 0.05$ considered as significant by comparing treated group with control group using Graph Pad Prism 4.0.

PATIENTS AND CLINICAL METHODS

4f.CLINICAL STUDY:

4f.1.Clinical trial Approval & Registration:

The Clinical trial was approved by the Institutional Ethics Committee (IEC) of National Institute of Siddha, Chennai 47 (NIS/13-IEC/2017-1-08/22-11-2017) and further registered in Clinical Trial Registry of India (CTRI).

4f.2.Study Centre:

Clinical study was conducted at AyothidossPandither Siddha Hospital, National Institute of Siddha (NIS), Tambaram Sanatorium, Chennai - 47. Necessary permission was obtained from the Administrative head to conduct the study.

4f.3.Study Population:

For Open Clinical trial, patients who were attending the OPD of NIS were inducted after obtaining informed consent from all of them. Totally 118 patientswere screened and among them 40 who complied with the inclusion criteria were included in the study.

4f.4.Subject Selection:

Patients reporting with symptoms of Kalanjagapadai will be subjected to screening using screening Proforma. Then they will be allowed for the study fulfilling the following criteria:

Inclusion Criteria

- Age : 20-65 years
- Sex : Both male and female, Transgender
- History of Insulin Dependent Diabetes Mellitus
- Itching (with or without)
- Erythema
- Scaling
- Auspitz sign +
- Candle crease sign +
- Willing to give specimen of blood for the investigation whenever required.
- Willing to take photograph
- Willing to participate in trial and signing consent by fulfilling the condition of Proforma.

Exclusion Criteria

- History of Insulin Dependent Diabetes Mellitus
- Pregnancy and lactation
- History of Psoriasis with evidence of any other skin disease or Evidences of secondary infection in the lesions.
- History of Psoriatic arthropathy
- History of Cardiac diseases
- History of Hansen's disease
- History of any other chronic illness

Withdrawal Criteria

- Intolerance to the drug and development of any serious adverse effect during drug trial.
- Poor patient compliance & defaulters
- Patient unwilling to continue the course of clinical Study.
- Occurrence of any other systemic illness.

4f.5.Informed consent:

To respect the rights of the study participants the information sheet containing entire details of the study was given to them. Then a written consent to participate in this study was obtained from the participants before the enrollment.

4f.6.Data collection:

Required information was collected from each patient by using the following forms:

Form – I Screening and selection Proforma

Form – II History taking Proforma

Form – III Clinical assessment Proforma

Form – IV Laboratory investigation Proforma

Form – V Consent form

Form – VI Withdrawal form

Form -VI-A Drug Compliance Form

Form – VII Patient information sheet

Form – VIII Dietary Advice Form

Form – IX Adverse Reaction Form / Pharmaco Vigilance Form

4f.7.Assessment of efficacy parameters:

Siddha parameters:

Changes in symptoms, envagaithervu, naadi, neerkuri and neikuri and manikadainool.

Clinical Assessment:

Macules, Papules, Pustules, Plaques, Erythema, Scaling,Candle-greasesign, Auspitzsign, Itching, Koebner'sphenomenon.

Laboratory Investigation:

Blood: - TC, DC**,** Hb, ESR, Blood sugar, Lipid profile etc.

Renal Function Tests:

Blood Urea, Serum Creatinine, Uric acid.

Liver Function Tests:

Serum total bilirubin, direct bilirubin, indirect bilirubin, Serum Alkaline phosphatase, SGOT, SGPT.

Urine:

Albumin, Sugar, Deposits.

4f.8.Study Enrolment:

- Patients reporting at the OPD with clinical feature of erythematous patches, silvery scaling are chosen for enrolment based on the inclusion and exclusion criteria.

- The enrolled patients will be informed about the study, trial drug, possible outcomes and the objectives of the study in the language and terms understandable to them and getting consent in the Informed Consent form (Form VI).
- Complete clinical history, complaints and duration, examination findings-- all would be recorded in the prescribed Proformas.
- Screening Form- I will be filled up, Form –II and Form –III will be used for recording the patients, history, clinical examination of symptoms and signs and laboratory investigations respectively. If there is any abnormal laboratory reports obtained then excluded from this study. Patients would be advised to take the trial drug and appropriate dietary advice (Form VIII) would be given according to the patients, perfect understanding.

4f.9.Conduct of the study:

Group I : Trail drug without yogam in OPD patients.

Group II : Trail drug with yogam in IPD patients.

4f.9.1.First day :

Agathiyar kulambu with 200mg with 30ml leaf juice of Sangankuppi (*Azima tetracantha*) quantity was administered at early morning as purgative (*Kazhichal* Medicine) before starting the treatment for restore equilibrium of dhoshams.

4f.9.2.Second day :

Oil bath with *Arakku thylam* had taken at early morning for restore equilibrium of udalthathus.

4f.9.3.Third day onwards from Sunday/Tuesday/Thursday for 48 days :

Internal Medicine: *Parangipattai Kudineer*, three times a day before food.

External Medicine: *Sivappu thylam*

4f.9..4.Advice for method of topical therapy :

Oil applied in psoriatic lesion by cotton for 4 hrs at 1pm to 5pm and take sunbath at 4pm to 5.30pm thereafter bath with warmwater used by greengram powder.

Yogam therapy (Agathavam Ettu) gave for IPD patients. Envagai Thervu was evaluvate before and after the treatment for 40 patients. Nei Kuri was evaluvate 0^{th}day,15^{th} day,49^{th} day of the treatment for opd and IPD patients. Manikadai Nool was measure before the treatment for 40 patients.

OPD patients are requested to visit the hospital once in 7 days. In each and every visit clinical assessment and prognosis were recorded. For IPD patients the clinical assessment and prognosis were recorded daily.

Laboratory investigations were done before and after the trial. For IPD patients, who are not in a position to stay in the hospital for a long time are advised to attend the OPD for further follow-up. At the end of the trial, the patients are advised to visit the OPD.

4f.9..5.Pharmaco-Vigilance (Adverse/serious adverse effects management):

If the trial patient develops any adverse reaction, he/she would be immediately withdrawn from the trial and he will be directed to take treatment in OPD of NIS. It will also be reported to the Pharmaco-vigilance committee of NIS. In case of emergency, the patients will be referred to nearby Government hospital for emergency management.

4f.9.6.Dermatology Life Quality Index (DLQI):

Recent studies have emphasized the association of psoriasis severity with impaired physical and public functioning as well as with the emotional state. The DLQI is calculated by summing the score of each question resulting in a minimum of 0 and a maximum of 30. The higher the score, the more quality of life is impaired.

4f.9.7.Outcome measures:

The outcome of the study was clinically observed by the PASI Score.

PASI Score: -

*** PASI 25** = 25% **(Poor)** reduction in the PASI Score in before and after treatment.

*** PASI 50 =** 50% **(Moderate)** reduction in the PASI Score in before and after treatment.

*** PASI 75 =** 75% **(Good)** reduction in the PASI Score in before and after treatment.

4f.9.8.Data analysis:

After enrolling the patients in the study, case report form book for patients will be maintained. Study No. and patient's No. will be entered on the top of the file for easy identification. Whenever the patients visit OPD during the study period, necessary entries will be made at the assessment forms. The screening forms will be filled separately. All forms will be further scrutinized by Senior Research Officer (Statistics) for logical errors and incompleteness of data to avoid any bias. No modification in the results is permitted for unbiased reports.

5. OBSERVATION AND RESULTS WITH STATISTICAL ANALYSIS

5.1.1.Authentication of the ingredients:

The ingredients of PPK were identified and authenticated by the Medicinal Botanist of NIS **(certificate number: NISMB3192018)**.

5.1.2.Purification of ingredients:

The raw drugs were purified as per the methods mentioned in the Siddha literatures. After purification, the ingredients are dried in the shade.

5.1.3.Preparation of PPK:

The raw drugs were purified and crushed into coarse powder.

5.2.Pharmacognostical Standardisation:

Getting the identification of the herbal ingredients, they were tested for macroscopical description.

5.2.1.Physico - Chemical Characterisation as per AYUSH portal :

Sample –ID **Parangipattai Kudineer Chooranam – PKC**

Figure.5.1.Sample Description

Table.5.1.Sample Description

State	Solid- Crude raw Material	Decoction- Water Extraction
Appearance	Greenish Brown	Reddish Brown
Nature	Hard Fibre/ Woody	Slightly viscous
Odor	Mild Characteristic	Mild Characteristic

5.2.2.Determination of pH

PH	4.5

5.2.3.Physico-Chemical analysis results:

s.no	**Parameters**	**Percentage**
1	Loss on drying	7.22 %
2	Total ash value	6.18%
3	Acid insoluble ash	1.73%
4	Water soluble ash	1.77%
5	Water soluble extraction	25.35%
6	Alcohol soluble extraction	19.62%

Table :5.2. Results of physicochemical parameters

Loss on drying indicates the moisture content. The total ash substance is the measure of inorganic substances present in the drug. High ash content proves its unsuitable nature to be used as drug. This formulation satisfy the Pharmacopoeial standards and as per the WHO Guidelines.

5.2.4.PARTICLE SIZE DETERMINATION :

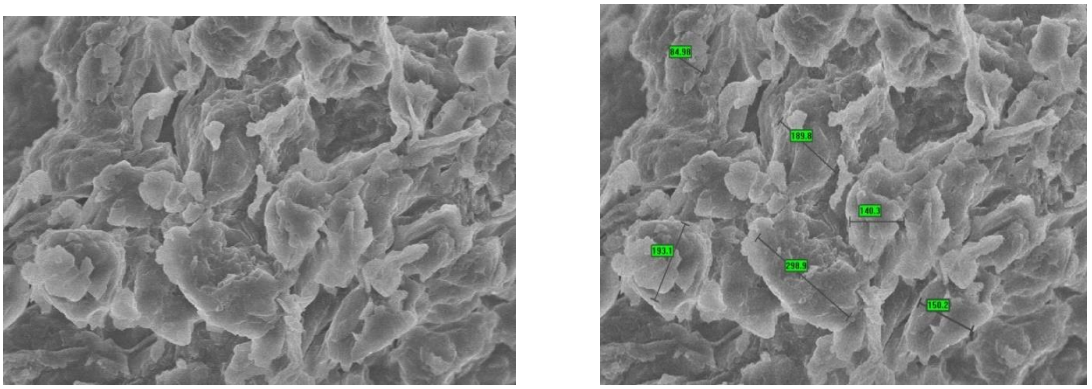


Figure.5.2.Electron Microscopic Observation of Particle Size for the Test Sample- PKC REPORT

Mean	**175.7**
Std. Deviation	**71.8**
Std. Error	**29.31**

Microscopic observation of the particle size analysis reveals that the average particle size of the sample was found to be 175.7 ± 71.8 µm

5.2.5.Microbiological contaminant study :

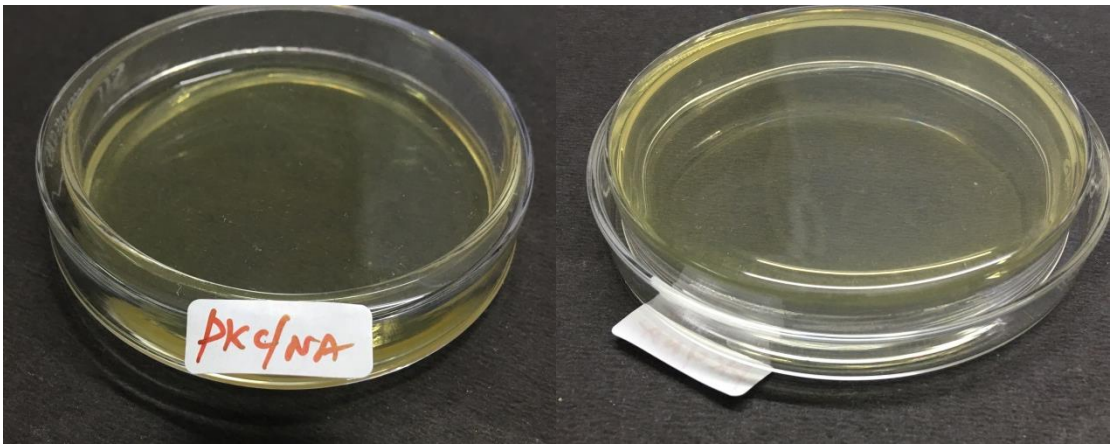


Figure.5.3.Sterility test by pour plate method

Observation

No growth was observed after incubation period. Reveals the absence of specific pathogen.

Result

No growth / colonies were observed in any of the plates inoculates with the test sample.

Test	**Result**	**Specification**	**As per AYUSH/WHO**
Total Bacterial Count	Absent	NMT 10^5CFU/g	As per AYUSH specification
Total Fungal Count	Absent	NMT 10^3CFU/g	

Table.5.3.Microbiological contaminant study

5.2.6.TLC & HPTLC analysis of aqueousextract of Parangipattai Kudineer Chooranam (PKC):

TLC Analysis at 366 nm **Track at All Wavelength**

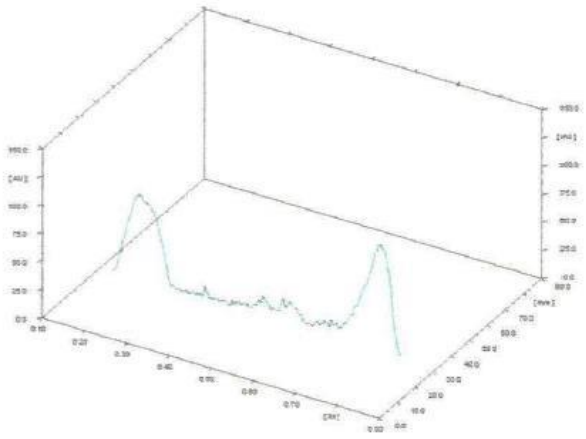


Figure.10.4.TLC Analysis

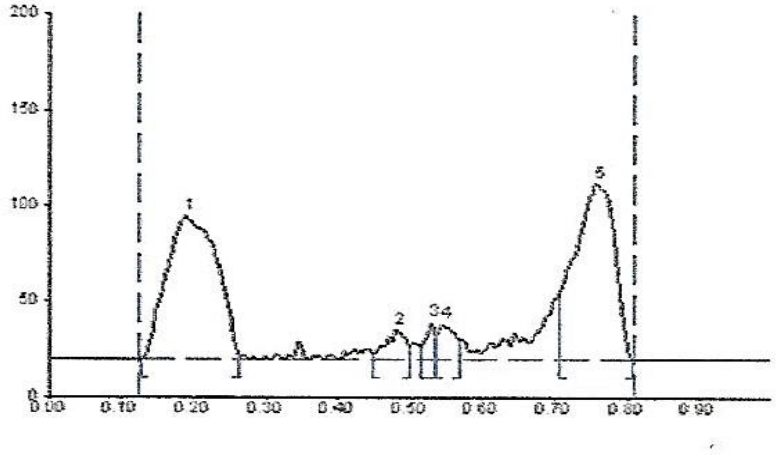


Figure.5.5. HPTLC finger printing of Sample PKC

Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %
1	0.05	0.9	0.07	191.9	46.49	0.09	0.5	2353.8	18.18
2	0.13	1.1	0.19	74.9	18.15	0.26	1.4	4861.0	37.55
3	0.45	3.2	0.48	15.7	3.82	0.50	6.9	386.7	2.99
4	0.52	7.2	0.53	19.4	4.70	0.54	12.6	210.9	1.63
5	0.54	13.1	0.55	18.6	4.52	0.57	10.2	403.2	3.11
6	0.71	35.7	0.76	92.2	22.33	0.81	0.5	4729.1	36.53

Table.5.4.HPTLC Peak Table

REPORT

HPTLC finger printing analysis of the sample PKC reveals the presence of six prominent peaks corresponds to presence of six versatile phytocomponents present with in it. Rf value of the peaks ranges from 0.05 to 0.71. Further the peak 2 and 6 occupies the major percentage of area of 37.55 and 36.53 % which denotes the abundant existence of such compound. Followed by this peak 1 and 3 occupies the percentage area of 18.18 and 3.11 %.

5.2.7.HEAVY METAL ANALYSIS BY AAS:

The observed results of heavy metal analysis are tabulated below in table

Name of the Heavy Metal	Absorption Max Λ max	Result Analysis	Maximum Limit
Mercury	253.7 nm	BDL	1 ppm
Lead	217.0 nm	1.185	10 ppm
Arsenic	193.7 nm	0.460	3 ppm
Cadmium	228.8 nm	BDL	0.3 ppm

BDL : Below Detection Limit

Table.5.5. Results of heavy metal analysis

REPORT AND INFERENCE :

- Results of the present investigation have clearly shows that the sample has no traces of heavy metal Mercury and cadmium . Further the results show the presence of Lead and Arsenic and cadmium at 1.185 and 0.460 ppm level.
- The reported heavy metal seems very low when compare to the allowed recommended limit.

5.2.8.PESITICIDE RESIDUE :

Pesticide Residue I.Organo Chlorine Pesticides	Sample PKC	AYUSH Limit (mg/kg)
Alpha BHC	BQL	0.1mg/kg
Beta BHC	BQL	0.1mg/kg
Gamma BHC	BQL	0.1mg/kg
Delta BHC	BQL	0.1mg/kg
DDT	BQL	1mg/kg
Endosulphan	BQL	3mg/kg
II.Organo Phosphorus Pesticides		
Malathion	BQL	1mg/kg
Chlorpyriphos	BQL	0.2 mg/kg
Dichlorovos	BQL	1mg/kg
III.Pyrethroid		
Cypermethrin	BQL	1mg/kg

BQL- Below quantification Limit

Table.5.6.Test Result Analysis Of The Sample PKC

Result:

The results showed that there were no traces of pesticides residues such as Organo chlorine, Organo phosphorus and pyrethroids in the sample PKC.

5.2.9.Aflatoxin Assay By TLC (B1,B2,G1,G2) :

Aflatoxin	Sample PKC	AYUSH Specification Limit
B1	Not Detected – Absent	0.5 ppm
B2	Not Detected – Absent	0.1 ppm
G1	Detected 0.005	0.5 ppm
G2	Not Detected – Absent	0.1 ppm

Table.5.7. Aflatoxin Assay By TLC

Result:

The results shown that there was no spots were been identified in the test sample loaded on TLC plates with respect to aflatoxins B1,B2 and G2 when compare to standard . Whereas presence of aflatoxin G1 were identified. This level of aflatoxins. G2 seems very low and further within the AYUSH prescribed limit of 0.5ppm AYUSH.

5.2.10.Test for Specific Pathogen:

Organism	Specification	Result	Method
E-coli	Absent	Absent	As per AYUSH specification
Salmonella	Absent	Absent	
Staphylococcus Aureus	Absent	Absent	
Pseudomonas Aeruginosa	Absent	Absent	

Table.5.8. Specific Pathogen

Observation

No growth was observed after incubation period. Reveals the absence of specific pathogen

Result

No growth / colonies were observed in any of the plates inoculated with the test sample.

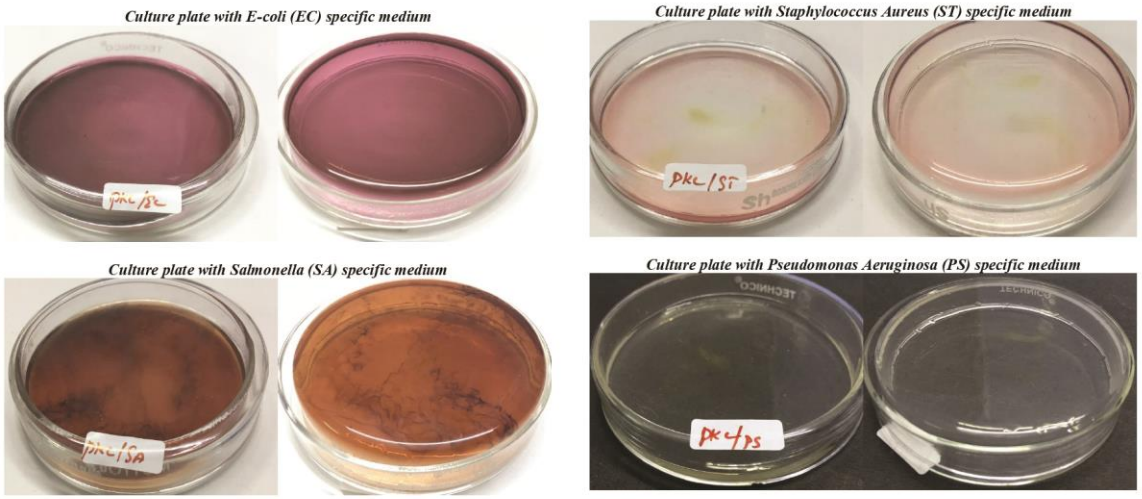


Figure.5.6. Culture plates of test for specific pathogens

5.3.Phytochemical Analysis:

S.no	Phytochemicals	Test Name	H20 Extract
1.	Alkaloids	Mayer's Test	-ve
		Wagner's Test	-ve
		Dragendroff's Test	-ve
		Hager's Test	-ve
2.	**Carbohydrates**	**Molisch's Test**	**+ve**
		Benedict's Test	**+ve**
3.	Glycoside	Modified Borntrager's Test	-ve
		Keller Killiani	-ve
4.	**Saponin**	**Froth Test**	**+ve**
		Foam Test	**+ve**
5.	Phytosterol	Salkowski's Test	-ve
6.	**Phenols**	**Ferric chloride Test**	**+ve**
7.	Tannins	Gelatin Test	-ve
8.	**Flavonoids**	**Alkaline Reagent Test**	**+ve**
		Lead Acetate Test	**+ve**
9.	Protein and amino acids	Xanthoproteic Test	-ve
10.	Diterpenes	Copper Acetate test	-ve
11.	Gum & Mucilage	Extract + Alcohol	-ve
12.	Fat & Fixed oil	Spot test	-ve
13.	**Quinones**	**NAOH+ Extract**	**+ve**

+ve /-ve present or absent if component tested

Table.5.9.Results of Phytochemical analysis

The above table shows the presence of all secondary metabolites (Flavonoids, Phenolic Compounds and Quinones, Saponins, Carbohydrates.

5.4.CHEMICAL ANALYSIS :

S.No	EXPERIMENT	OBSERVATION	INFERENCE
1.	Appearance of sample	Dark brown in Colour	**Brown**
2.	**Test for Silicate:** c. A little (500mg) of the sample is shaken well with distilledwater. d. A little(500mg) of the sampleis shaken well with con. HCl/Con. H_2So_4	Insoluble	Absence of Silicate
3.	**Action of Heat:** A small amount (500mg) of the sample is taken in a dry test tube and heated gently at first and then strong.	White fumes evolved No Brown fumes	Absence of Carbonate , Nitrate
4.	**Ash Test:** A filter paper is soaked in a mixture of sample and dil. cobalt nitrate solution and introduced into the Bunsen flame and ignited.	No Yellow colour flame appeared	Absence of Sodium

S.No	EXPERIMENT	OBSERVATION	INFERENCE
1.	**Test For Sulphate:** 2ml of the above-prepared extract was taken in a test tube and 2ml of 4% dil. ammonium oxalate solution was added.	No Cloudy appearance	Absence Sulphate

2.	**Test For Chloride:** 2ml of the above-prepared extracts was added with 2ml of dil-HNO_3 until the effervescence ceases off. Then 2 ml of silver nitrate solution was added.	Presence of Cloudy appearance	**Chloride present**
3.	**Test For Phosphate:** 2ml of the extract was treated with 2ml of con.HNo3 and 2ml of dil. ammonium molybdate solution.	Cloudy Yellow appearance present	**Presence of Phosphate**
4.	**Test For Carbonate:** 2ml of the extract was treated with 2mldil. magnesium sulfate solution	Presence of Cloudy appearance	**Carbonate Present**
5.	**Test For Sulphide:** 1gm of the substance was treated with 2ml of the con.HCL	Rotten Egg Smelling gas was not evolved	Sulphide absent

Test For Acid Radicals

6.	**Test For Fluoride & Oxalate:** 2ml of the extract was added with 2ml of dil. Acetic acid and 2ml dil. calcium chloride solution and heated**.**	No Cloudy appearance	Absence of fluoride and oxalate
7.	**Test For Nitrite:** 3drops of the extract was placed on a filter paper, on that-2 drops of dil. acetic acid and 2 drops of dil. Benzidine solution wasplaced.	Characteristic changes not appeared	Nitrite absent

8.	**Test for Borate:** 2 pinches of the substance is made into paste by using sulphuric acid and alcohol (95%) and introduced into the blue flame	Bluish green colour flame not appeared	Absence of borate

Test For Basic Radicals

1.	**Test For Lead:** 2ml of the extract was added with 2ml of dil. potassium iodine solution.	Yellow Precipitate was not obtained.	Lead absen t
2.	**Test For Copper:** One pinch (50mg) of substance was made into a paste with con. HCl in a watch glass and introduced into the non- luminous part of the flame.	The blue colour precipitate formed.	Copper Absent
3.	**Test For Aluminium:** In the 2ml of extract dil. sodium hydroxide was added in 5 drops toexcess.	Yellow colour was not formed	Aluminium absent

4.	**Test For Iron:** c. To the 2ml of extract add 2ml of dil. ammoniumsolution d. To the 2ml of extract, 2ml thiocyanate solution and 2ml of con HNo3 is added	Absence of brown precipitate Red colour formed	**Iron Present**
5.	**Test For Zinc:** In 2ml of the extract dil. sodium hydroxide solution was added in 5 drops to excess and dil. Ammonium chloride wasadded.	White precipitate was formed	**Zinc Present**
6.	**Test For Calcium:** 2ml of the extract was added with 2ml of 4% dil. ammonium oxalate solution	No Cloudy appearance and white preciptitate is obtained	Absence of Calcium
7.	**Test For Ammonium:** In 2ml of extract 1 ml of Nessler's reagent and excess of dil. sodium hydroxide solution was added.	Brown colour not formed	Ammonium absent
8.	**Test For Potassium:** A pinch (25mg) of substance was treated with 2ml of dil. sodium nitrite solution and then treated with 2ml of dil. cobalt nitrate in 30% dil. glacial acetic acid.	No Yellowish precipitate formed	Absence of Potassium

9.	**Test For Sodium:** 2 pinches (50mg) of the substance was made into a paste by using HCl and introduced into the blue flame of Bunsen burner.	Yellow colour flame not appeared	Sodium absent
10.	**Test For Mercury:** 2ml of the extract was treated with 2ml of dil. sodium hydroxide solution.	Yellow precipitate not formed	Mercury absent
11.	**Test For Arsenic:** 2ml of the extract was treated with 2ml of dil. sodium hydroxidesolution.	Brownish red precipitate not formed	Arsenic absent

OTHER CONSTITUENTS

1.	**Test For Starch:** 2ml of extract was treated with weak dil. iodine solution	No Blue colour developed	Absence of Starch
2.	**Test For Reducing Sugar:** 5ml of Benedict's qualitative solution was taken in a test tube and allowed to boil for 2minutesandadded8to10dropsofthe extract and again boil it for 2 minutes.	The was no specific change in colour	Reducing sugar absent
3.	**Test For The Alkaloids**: c) 2ml of the extract is treated with 2ml of dil. Potassium iodide solution. d) 2ml of the extract is treated with 2ml of dil. picricacid.	Reddish brown precipitation formed Yellow precipitatio n formed	**Alkaloid Present**

4.	**Test For Tannic Acid:** 2ml of the extract was treated with 2ml of dil. ferric chloride solution	Black precipitate formed	**Tannic acid present**
5.	**Test For Amino Acid:** 2 drops of the extract were placed on a filter paper and dried well, and then 20ml of Biuret reagent was added to it.	Violet colour not developed	Amino acid absent
6.	**Test for Type of Compound:** 2 ml of the extract is treated with 2 ml of ferric chloride solution	Green color developed	**Presence of oxyquinole epinephrine and pyro catechol**.

The above table shows the presence of Chloride,Phosphate, Carbonate , Iron, Zinc , Alkaloids, Tannic acid and oxyquinole epinephrine and pyro catechol.

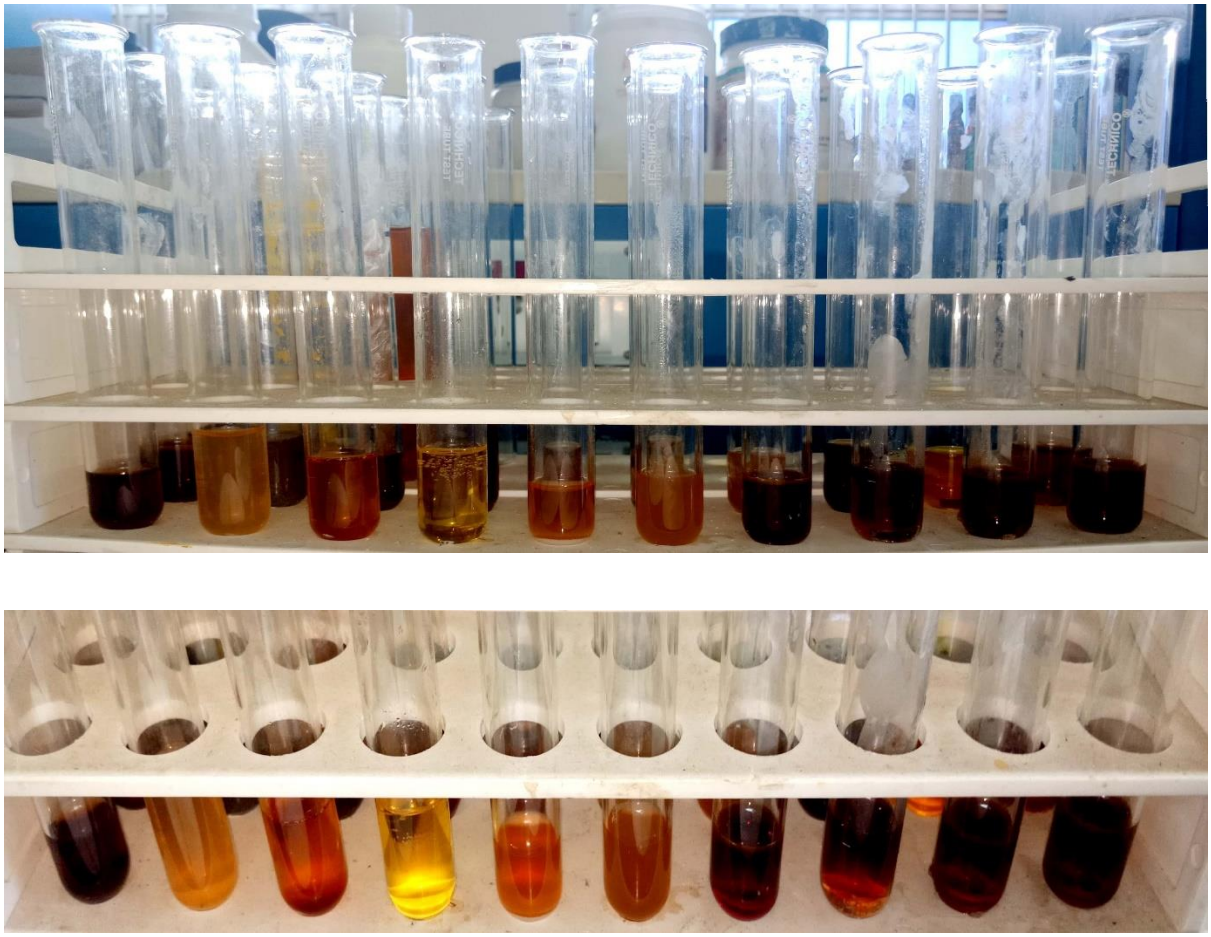


Figure.5.7. Chemical Analysis

5.5.PHARMACOLOGICAL SCREENING OF PARANGIPATTAI KUDINEER CHOORANAM :

5.5.1.In-vitro Anti-Inflammatory Activity by Protein (Albumin) denaturation Assay

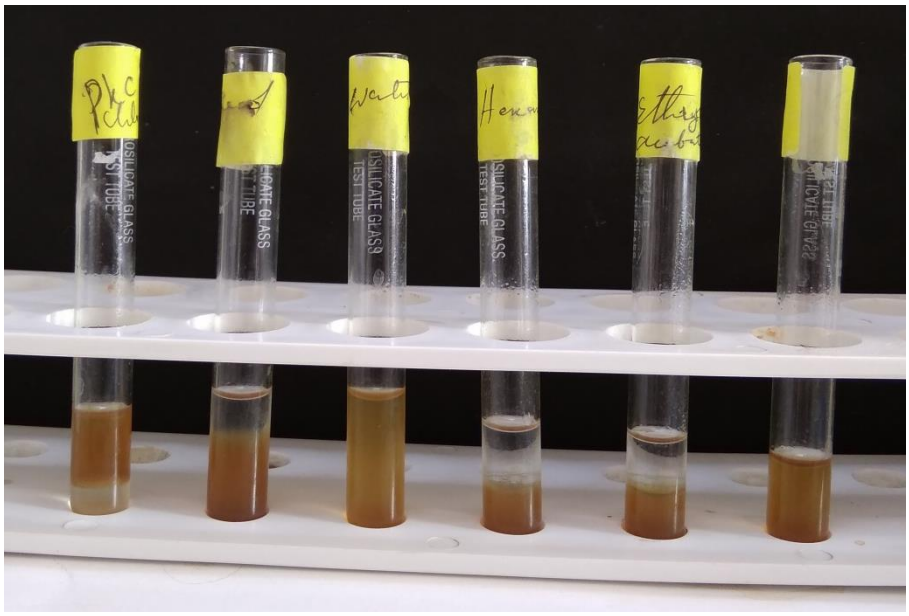


Figure.5.8. Sample Description

Solubility Profile of PKC		
S.No	**Solvent**	**Observation**
1	Chloroform	Insoluble
2	Ethanol	Slightly soluble
3	Water	Soluble
4	Ethyl acetate	Insoluble
5	DMSO	Soluble

Table.5.10.Solubility Profile

Statistical analysis

Results are expressed as Mean ± SD. The difference between experimental groups was compared by One-Way Analysis Of Variance (ANOVA) followed by Dunnet Multiple comparison test.

FINAL RESULT

Concentration in µg/ml	Percentage Inhibition of Protein Denaturation
PKC 100	16.09 ± 0.58
PKC 200	24.33 ± 0.83
PKC 300	37.11 ± 0.71
PKC 400	45.97 ± 2.18
PKC 500	61.2 ± 1.84
Diclofenac sodium (100 µg)	99.5 ± 0.38

Table.5.11.Each value represents the mean ± SD. N=3

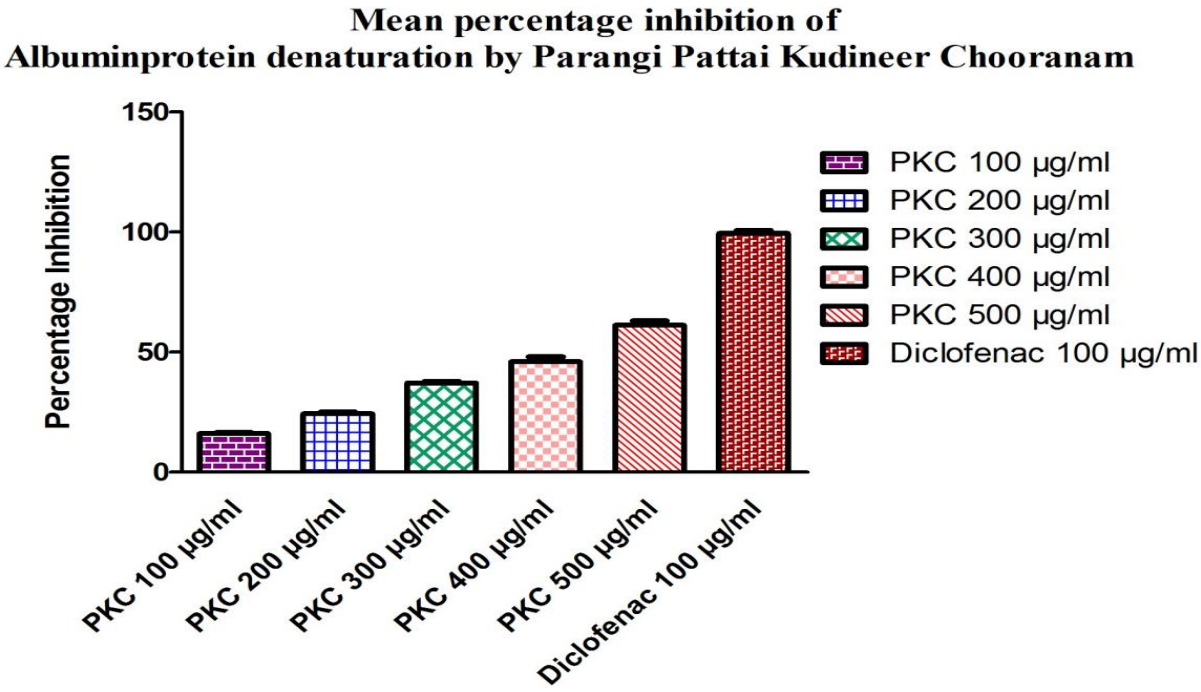


Figure.5.9. Percentage Inhibition of Protein Denaturation by PKC and Standard

Result Analysis

The result obtained from the present clearly indicates that the test drug PKC was effective in inhibiting heat induced albumin denaturation. Maximum percentage inhibition of about 61.2 ± 1.84% was observed at 500 µg/ml when compare to that of the Diclofenac sodium, a standard anti-inflammatory agent with the maximum inhibition 99.5 ± 0.38 at the concentration of 100 µg/ml.

Conclusion

From the result of the study it was concluded that the test drug PKC possess significant anti-inflammatory property in protein denaturation assay.

5.5..2.In vitro Immunomodulatory Activity of Siddha formulation *Parangipattai Kudineer Chooranam* (PKC) in RAW Macrophage Cell line :

Immunomodulatory Evaluation Report

Concentration (µg/ml)	Concentration of Nitrites (µg)
Control (LPS1µg/mL)	1153 ± 28.15
PKC 50 µg	506.7 ± 4.509
PKC 100 µg	444.3 ± 9.504
PKC 200 µg	230 ± 13.75

Table.5.12. Effect of Siddha Formulation PKC on Nitrite level in RAW 264.7 Cell line.

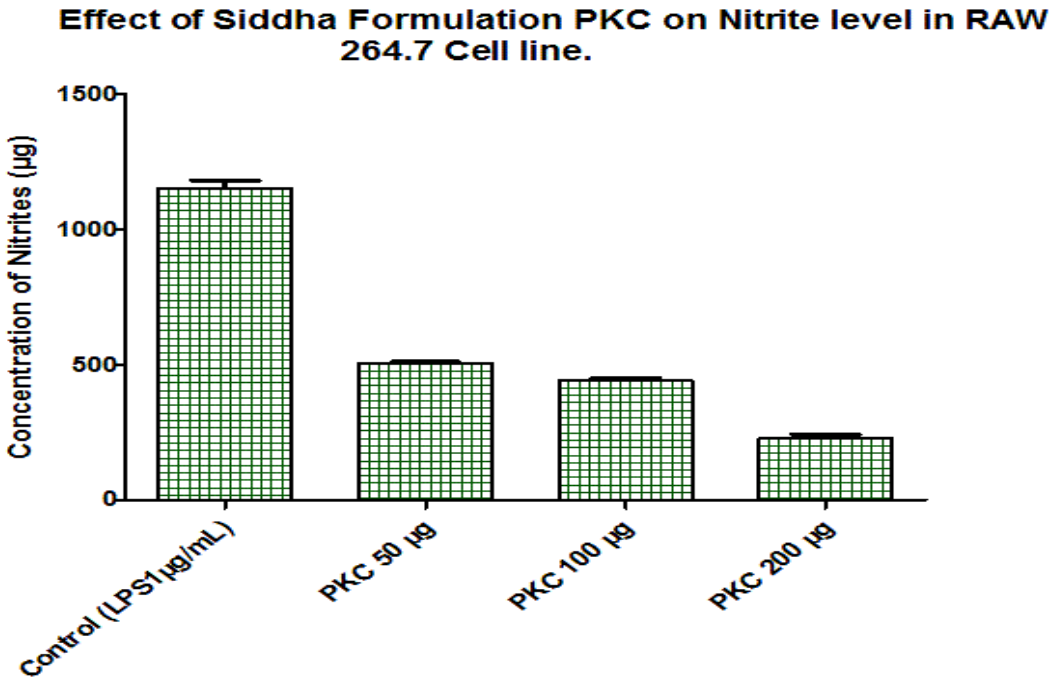


Figure.5.10. Effect of Siddha Formulation PKC on Nitrite level in RAW 264.7 Cell line.

S.No	Concentration in µg/ml	% cell Viability
1	Control (LPS1µg/mL)	95.98 ± 1.90
2	PKC 50 µg	82.3 ± 2.18
3	PKC 100 µg	65.88 ± 3.33
4	PKC 200 µg	47.3 ± 0.60

Table.5.13.Effect of PKC on Cell viability in RAW 264.7 Cell line

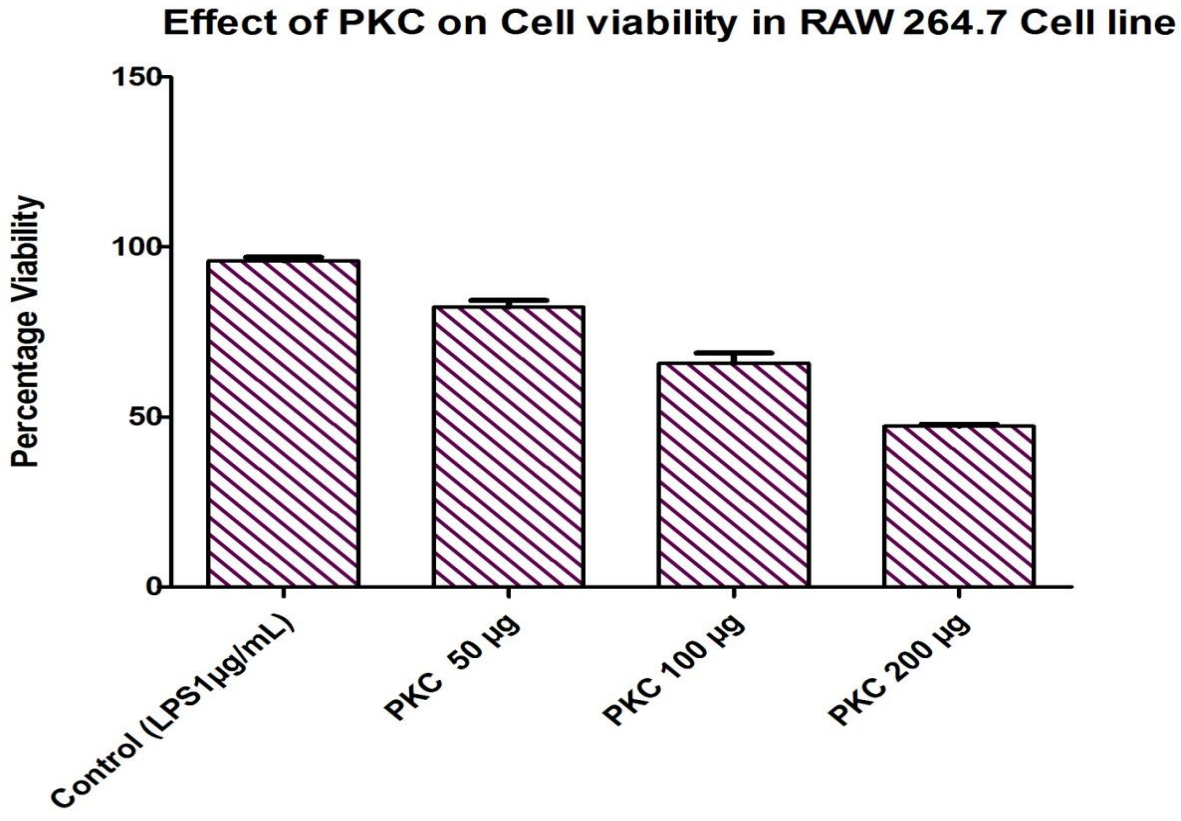


Figure.5.11. Effect of PKC on Cell viability in RAW 264.7 Cell line

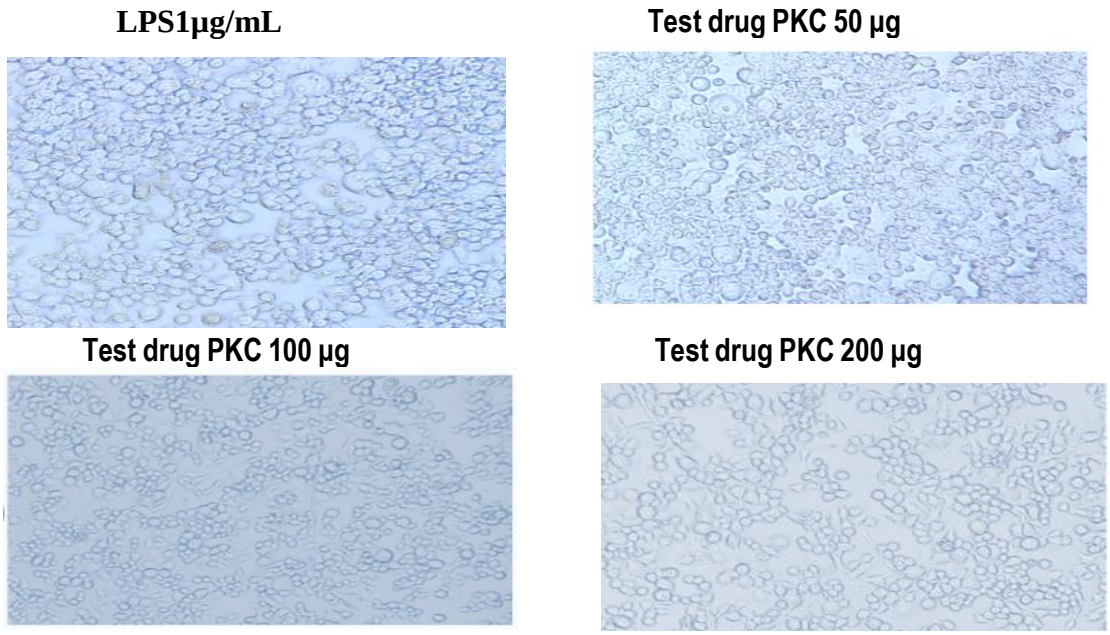


Figure.5.12.LPS induced proliferation in Macrophage cell line RAW 264.7

RESULT

It was observed that there was dose dependent decrease in the nitrite level in RAW 264.7 medium incubated with test drug at the concentration ranges from 50 to 200 µg/ml. Lipopolysaccharide (LPS) (1µg/mL) treated well was served as a control with maximum nitrite level of about 1153 ± 28.15 µg. The formulation PKC at the dose of 50 µg/ml shown a significant decrease in nitrite level of about 506.7 ± 4.50 µg similarly at the concentration of 100 µg/ml it shows 444.3 ± 9.504 µg and the maximum percentage decrease of nitrite level of about 230 ± 13.75 µg were observed at 200 µg/ml. The reuslt obtained from the study reveals that the percentage of cell viability of macrophase cell line decreases with increase in concentration of the test drug PKC Least viability of cell was observed at the concentration of 200µg/ml shows 47.3 ± 0.60 %.

Observation

The test drug PKC has significantly reduced the nitrite level at the concentration ranges from 50 to 200 µg/ml. Hence from the data's it was concluded that the formulation PKC possess remarkable immunomodulatory property.

5.5.3.In vitro Anti-proliferative Activity of Siddha formulation *Parangipattai Kudineer Chooranam*(PKC) in HaCaT cell line using MTT assay :

Table.5.14.Effect of Test drug PKC on Cell viability of HaCaT cell line

S.No	Concentration in µg/ml	% cell Viability
1	10	80.33 ± 10.26
2	50	64.91 ± 10.02
3	100	52.56 ± 4.789
4	150	40.08 ± 11.48
5	200	18.83 ± 10.16
6	250	11.62 ± 8.402

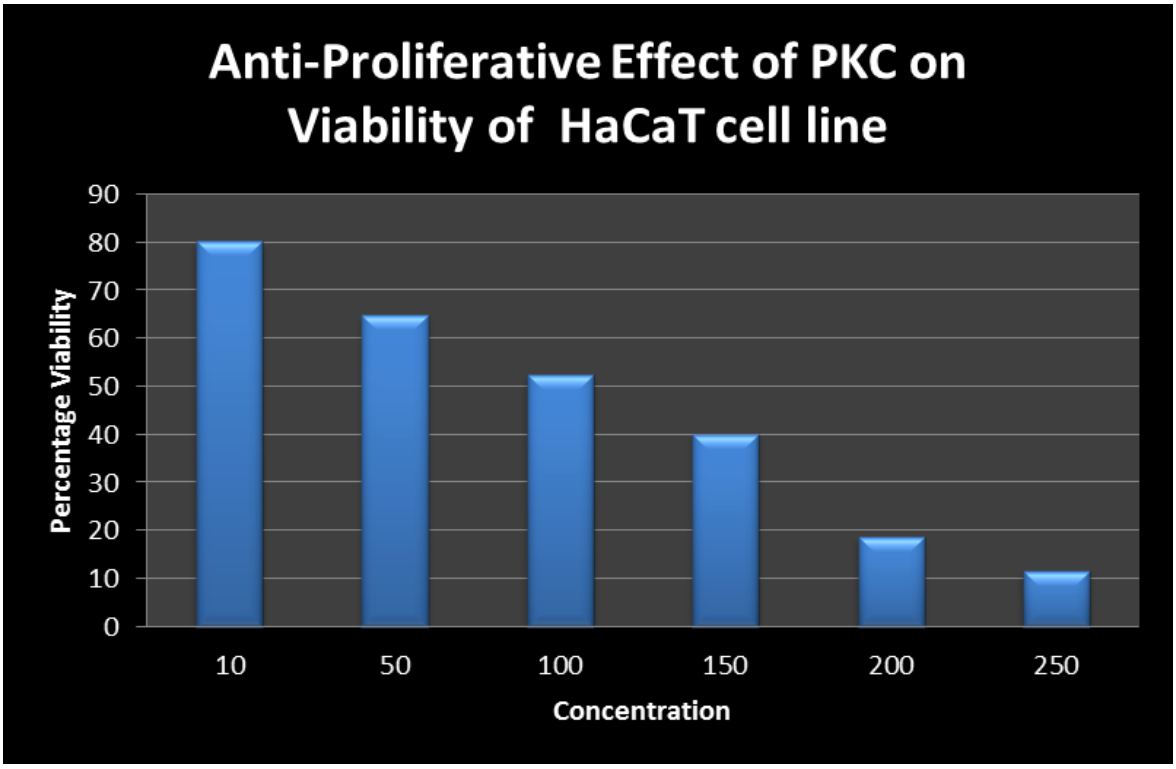


Figure.5.12. Effect of Test drug PKC on Cell viability of HaCaT cell line

Table.5.15.Effect of Test drug PKC on Cell death of HaCaT cell line

S.No	Concentration in µg/ml	% cell Death
1	10	19.57 ± 10.33
2	50	35.04 ± 9.975
3	100	47.37 ± 4.829
4	150	59.88 ± 11.43
5	200	81.11 ± 10.14
6	250	88.33 ± 8.424

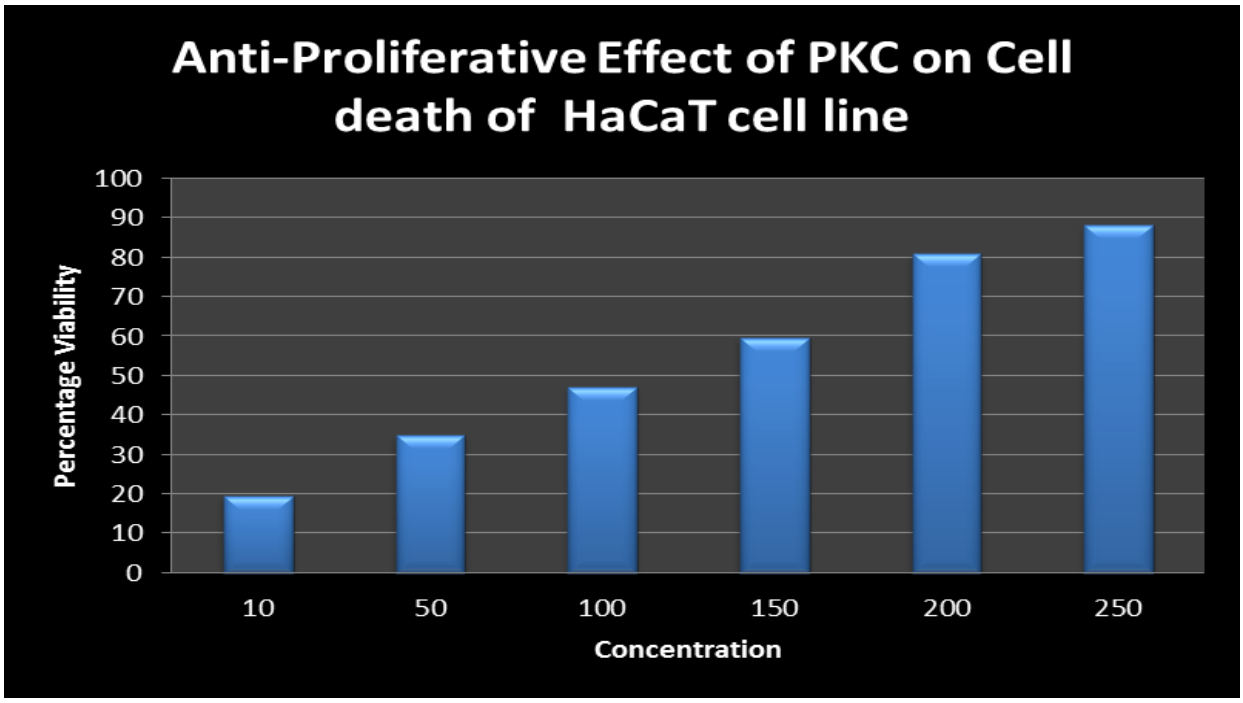
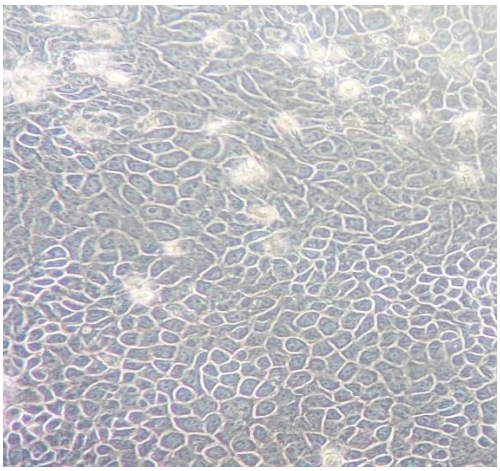


Figure.5.13. Effect of Test drug PKC on Cell death of HaCaT cell line

IC 50 Value of PKC

IC 50 Value of PKC	**106.9 ± 26.31 µg/ml**

HaCaT Control Cells



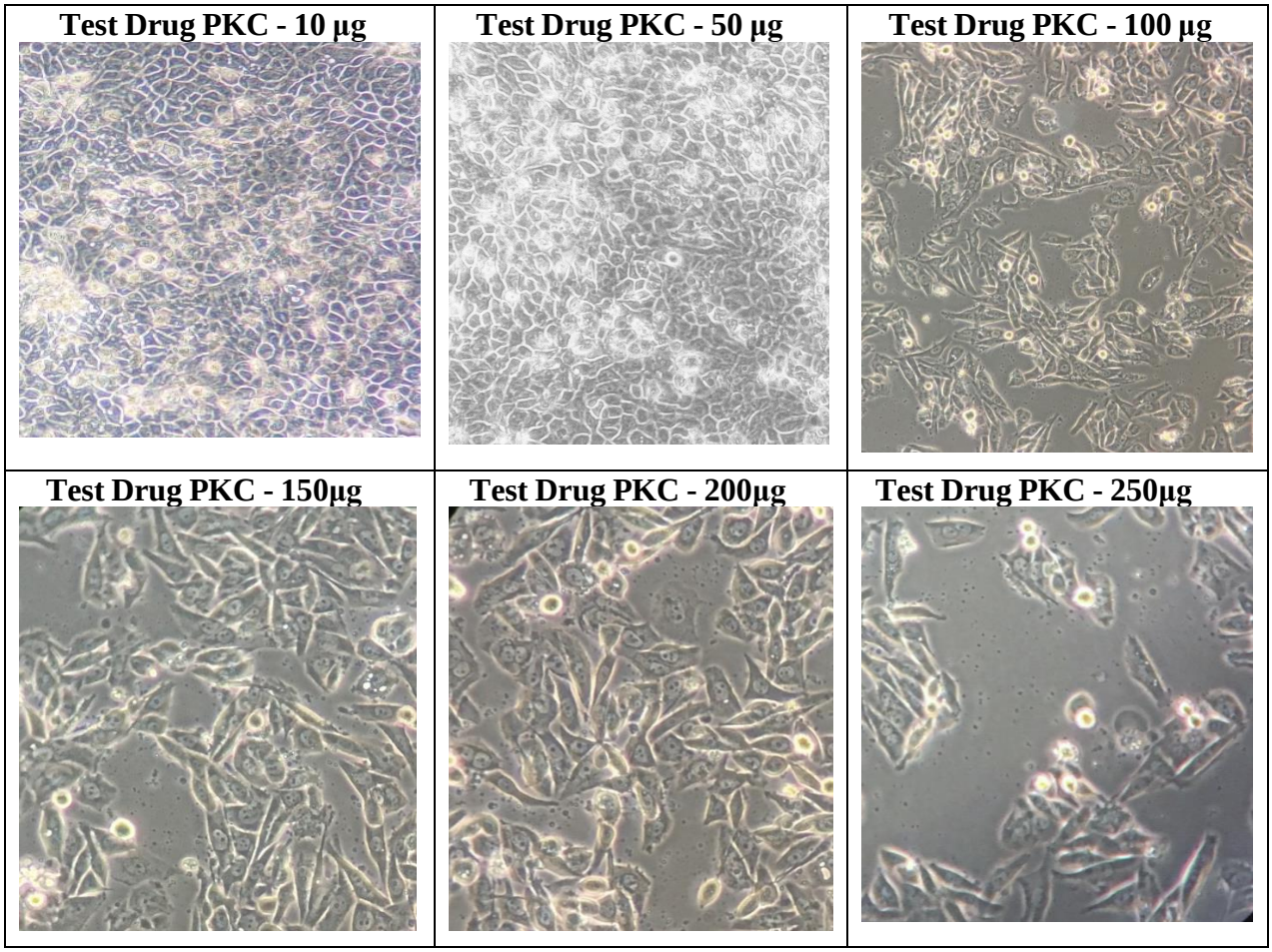


Figure.5.14.Effect of Test drug PKC on HaCaT cell line

Result and Discussion

In-vitro anti-proliferative evaluation of test drug PKC on the cell viability against HaCaT keratinocyte cell linewas performed at varying concentration ranges from 10 to 250 µg/ml .The reuslt obtained from the study reveals that the percentage of cell viability of HaCaT celline line viability decrease with increase in concentration of the test drug PKC. Least viability of cell was observed at the concentration of 250µg/ml shows 11.62 ± 8.402 %, followed by this 200µg/ml shows 18.83 ± 10.16 %, similarly 150, 100,50 and 10 µg/ml shows 40.08 ± 11.48,52.56 ± 4.789,64.91 ± 10.02 and 80.33 ± 10.26 % cell viability in MTT assay. The corresponding IC50 value was found to be 106.9 ± 26.31 µg/ml.

5.5.4.Docking analysis :
Molecular Docking Study Report

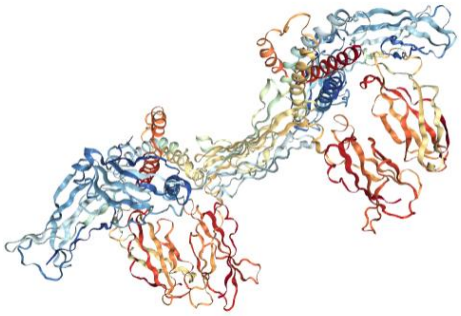
Table.5.16.Target Details

PDB	**Name of the Target**
1P9M	IL- 6
2AZ5	TNF-alpha
1NSI	Nitric Oxide Synthase

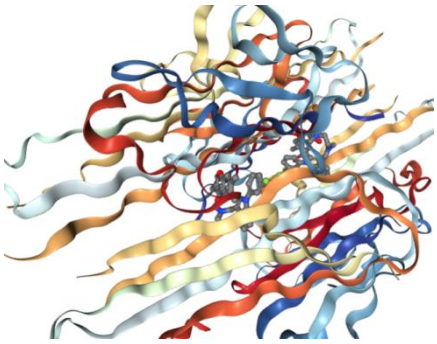
Crystalline structure of the target proteins IL- 6(1P9M), TNF-alpha (2AZ5) and Nitric Oxide Synthase (1NSI) was retrieved from protein data bank and protein clean-up process was done and essential missing hydrogen atom were been added. Different orientation of the lead molecules with respect to the target protein was evaluated by Autodock program and the best dock pose was selected based on the interaction study analysis.

Figure.5.15.RECEPTOR STRUCTURE

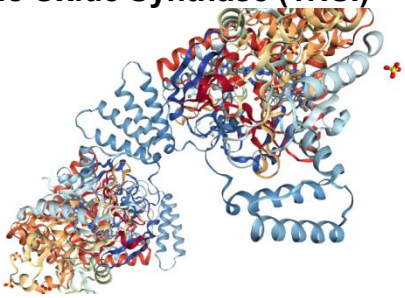
IL- 6(1P9M)



TNF-alpha (2A 5)



Nitric Oxide Synthase (1NSI)



Ligand Properties and Docking Score

Table.5.17.Ligand Properties of the Compounds selected for docking

Compound	Molar weight g/mol	Molecular Formula	H Bond Donor	H Bond Acceptor	Rotatable bonds
Anisaldehyde	136.148	C8H8O2	0	1	2
Berberine	336.361	C20H18NO4	0	4	2
Kaempferol	286.239	C15H10O6	4	6	1
Protocatechuic acid	153.112	C7H6O4	3	1	1
Nimbolide	466.523	C27H30O7	0	7	4
Picein	298.289	C14H18O7	4	7	4
Tacrolimus	773.992	C44H69NO12	3	12	7

Table.5.18 .Summary of the molecular docking studies of the lead compounds against IL-6

Compounds	Binding Free energy Kcal/mol	Inhibition constant Ki µM (*mM)(**nM)	Intermolecular energy Kcal/mol	Total Interaction Surface
Anisaldehyde	-3.77	1.72	-4.37	382.53
Berberine	-6.20	28.66*	-0.64	750.61
Kaempferol	-6.38	20.95*	-6.85	626.40
Protocatechuic acid	-4.64	393.85*	-4.93	406.07
Nimbolide	-8.40	691.97*	-9.17	790.68
Picein	-6.69	12.40*	-7.37	703.68
Tacrolimus	-5.65	72.15**	-4.53	620.79

Table.5.19.Summary of the molecular docking studies of the lead compounds against TNF-Alpha

Compounds	Binding Free energy Kcal/mol	Inhibition constant Ki µM (*mM)(**nM)	Intermolecular energy Kcal/mol	Total Interaction Surface
Anisaldehyde	-2.95	6.88	-3.55	375.95
Berberine	-4.75	331.70*	-5.36	530.60
Kaempferol	-4.96	230.90*	-5.47	433.93
Protocatechuic acid	-3.85	1.57*	-4.05	324.45
Nimbolide	-6.61	14.20*	-7.36	556.19
Picein	-5.15	168.60*	-5.66	483.95
Tacrolimus	-9.29	155.40**	-8.44	721.58

Table.5.20.Summary of the molecular docking studies of the lead compounds against Nitric oxide synthase

Compounds	Binding Free energy Kcal/mol	Inhibition constant Ki µM (*mM)(**nM)	Intermolecular energy Kcal/mol	Total Interaction Surface
Anisaldehyde	-4.15	908.35*	-4.75	420.96
Berberine	-5.86	503.20*	-6.47	683.60
Kaempferol	-5.73	63.42*	-6.16	607.80
Protocatechuic acid	-4.31	694.39*	-4.67	423.53
Nimbolide	-6.29	24.39*	-7.06	641.73
Picein	-6.19	29.21*	-6.85	626.87
Tacrolimus	-10.41	23.42**	-10.34	944.35

Table.5.21.Amino acid Residue Interaction of Lead and Standard against IL- 6 – PDB 1P9M

No of Interactions	Lead / Standard	Amino Acid Residue- Binding						
1	Anisaldehyde	134 THR	136 PHE	152 ALA	157 PRO			
2	Berberine	129 GLU	135 ASN	136 PHE	152 ALA	154 ARG	157 PRO	158 THR
1	Kaempferol	104 PRO	129 GLU	130 THR	134 THR	135 ASN	136 PHE	157 PRO
0	Protocatechuic acid	150 CYS	153 LYS	156 THR	159 SER	160 CYS	161THR	
1	Nimbolide	129 GLU	130 THR	134 THR	136 PHE	157 PRO		
0	Picein	129 GLU	130 THR	135 ASN	152 ALA	154 ARG		
3	Tacrolimus	109 ASN	123 GLU	125 ASP	157 PRO	158 THR		

Amino acids such as 109 ASN, 157 PRO and 158 THR are the core residue involved in mediating the IL-6 activity .Binding of lead compounds with this core residue may inhibit the activity .Out of six compound's Berberine has 2 interactions similar to that of the standard Tacrolimus. Other compounds such as Anisaldehyde , Kaempferol and Nimbolide has one interaction similar to that of the standard. Hence these compounds possess promising IL-6 inhibition activity

Table.5.22.Amino acid Residue Interaction of Lead and Standard against TNF-alpha (2AZ5)

No of Interactions	Lead / Standard	Amino Acid Residue- Binding						
4	Anisaldehyde	59 TYR	61 GLN	119 TYR	151 TYR			
3	Berberine	15 HIS	59 TYR	119 TYR	151 TYR			
3	Kaempferol	59 TYR	119 TYR	120 LEU	151 TYR			
3	Protocatechuic acid	59 TYR	61 GLN	119 TYR	151 TYR			
3	Nimbolide	59 TYR	61 GLN	119 TYR	151 TYR	155 ILE		
4	Picein	15 HIS	59 TYR	61 GLN	119 TYR	149 GLN	151 TYR	
4	Tacrolimus	57 LEU	59 TYR	61 GLN	119 TYR	149 GLN	151 TYR	155 ILE

Amino acids such as 59 TYR, 61 GLN,119 TYR and 151 TYR are the core residue involved in mediating the TNF- Alpha activity. Binding of lead compounds with this core residue may inhibit the activity. Out of six compound's Picein and Anisaldehyde has 4 interactions similar to that of the standard Tacrolimus. Other compounds such as Berberine, Kaempferol, Protocatechuic acid and Nimbolide has three interaction similar to that of the standard. Hence these compounds possess promising TNF- alpha inhibition activity.

Table.5.23.Amino acid Residue Interaction of Lead and Standard against Nitric Oxide Synthase

No of Interactions	Lead / Standard	Amino Acid Residue- Binding								
4	Anisaldehyde	374 MET	377 GLN	381 ARG	467 PRO					
3	Berberine	381 ARG	461 TRP	462 ILE	463 TRP	465 VAL				
3	Kaempferol	381 ARG	461 TRP	463 TRP	465 VAL					
1	Protocatechuic acid	374 MET	462 ILE	463 TRP	467 PRO					
3	Nimbolide	381 ARG	462 ILE	463 TRP	465 VAL	467 PRO				
4	Picein	381 ARG	461 TRP	463 TRP	465 VAL	467 PRO	476 PHE			
6	Tacrolimus	118 SER	374 MET	377 GLN	381 ARG	461 TRP	462 ILE	465 VAL	467 PRO	476 PHE

(1NSI)

Amino acids such as 374 MET ,377 GLN,381 ARG,461 TRP, 465 VAL and 467 PRO are the core residue involved in mediating the Nitric oxide synthase activity. Binding of lead compounds with this core residue may inhibit the activity . Out of six compound's Picein and Anisaldehyde has 4 interactions similar to that of the standard Tacrolimus. Other compounds such as Berberine, Kaempferol and Nimbolide has three interaction similar to that of the standard. Hence these compounds possess promising Nitric oxide synthase enzyme inhibition activity.

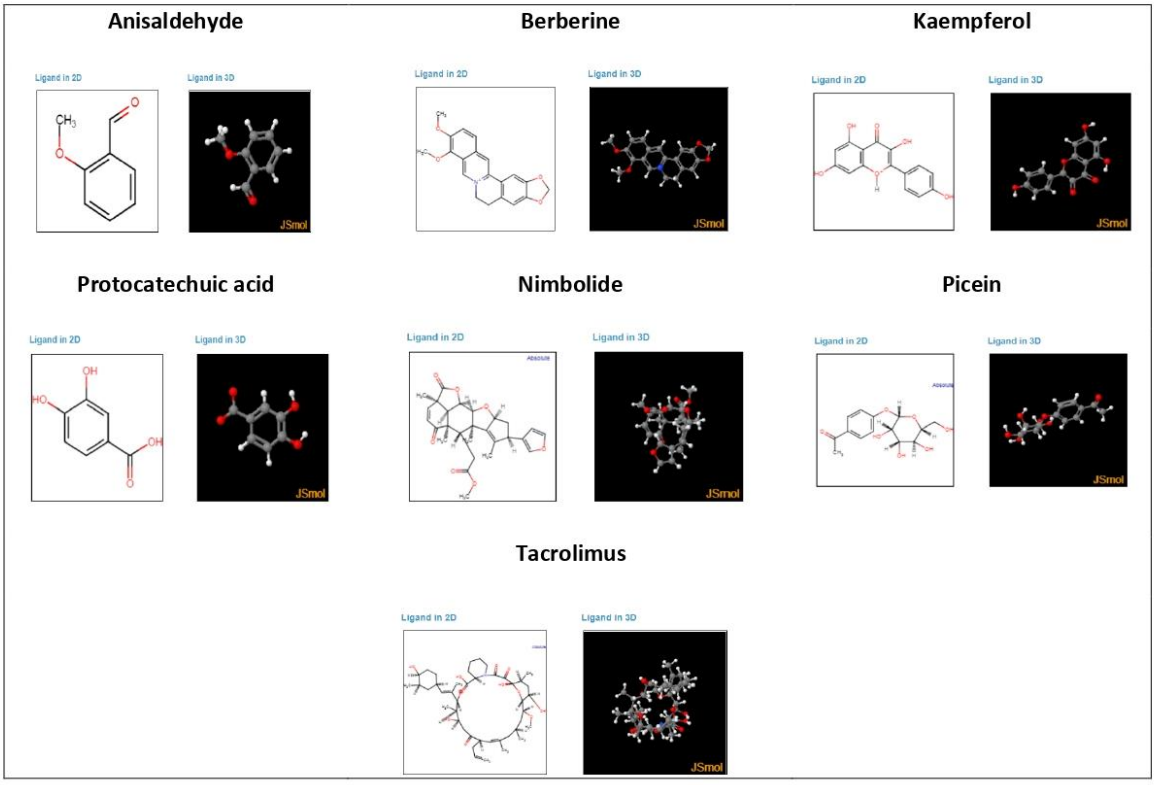
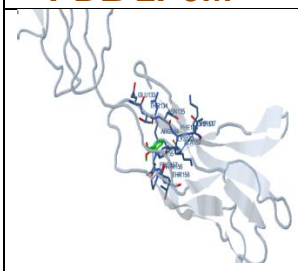
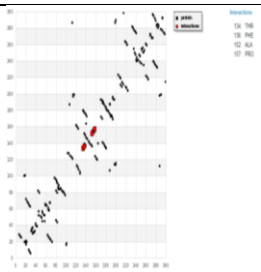
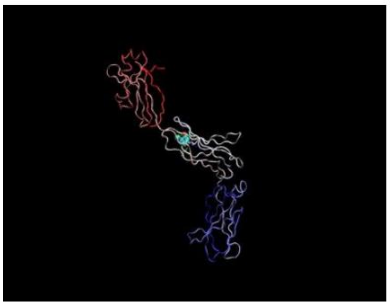
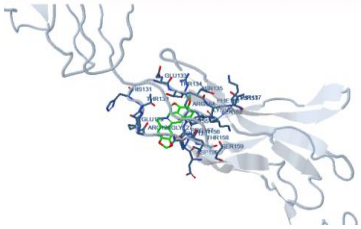
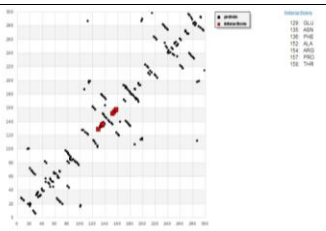
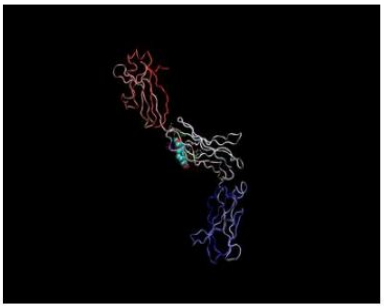
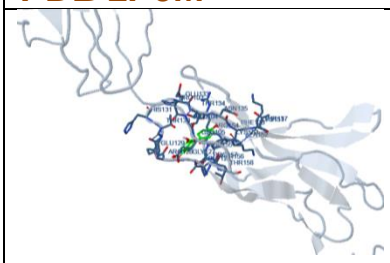
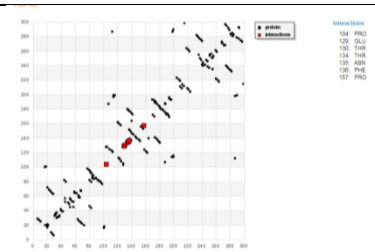
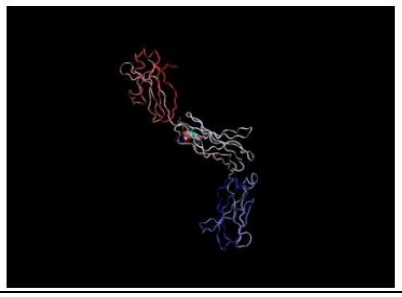
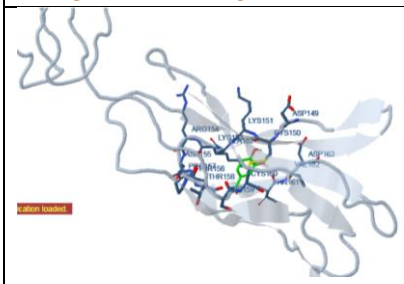
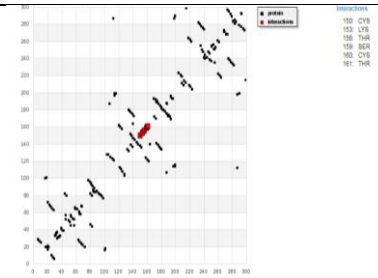
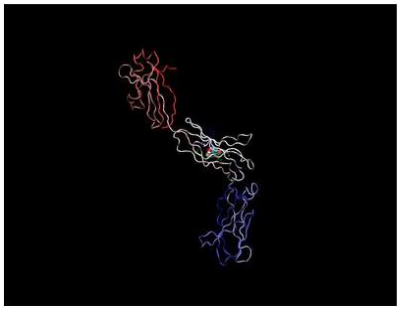


Figure.5.1 .2D and D Structure of lead Compounds

Figure.5.17.FINAL DOCKING REPORT IL-6 :

Anisaldehyde with IL- 6 – PDB 1P9M	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Berberine with IL- 6 – PDB 1P9M	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Kaempferol with IL- 6 – PDB 1P9M	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Protocatechuic acid with IL- 6 – PDB 1P9M	*HB Plotting Analysis*	*Receptor Ligand Complex*
		

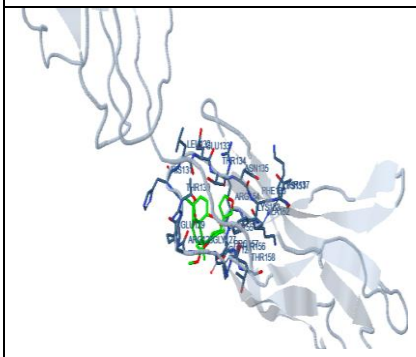
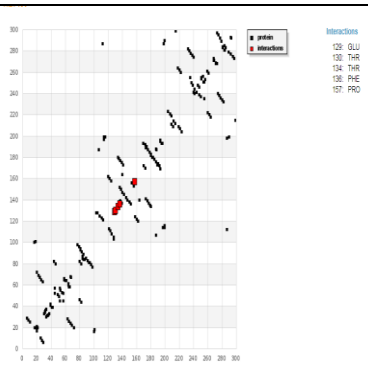
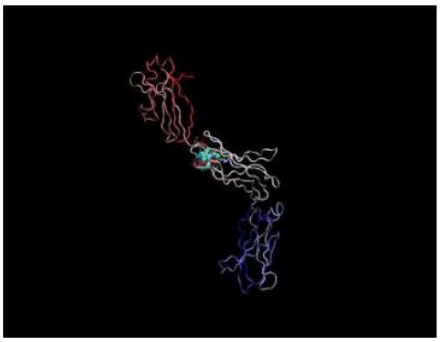
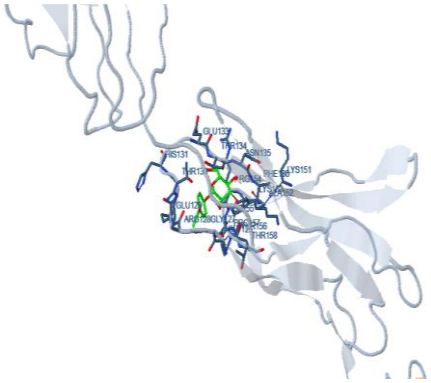
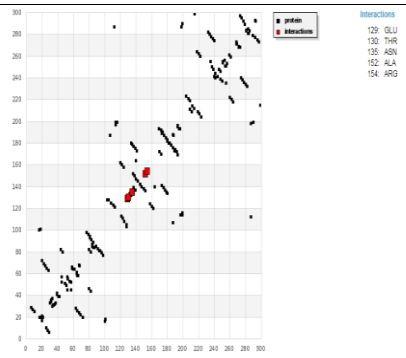
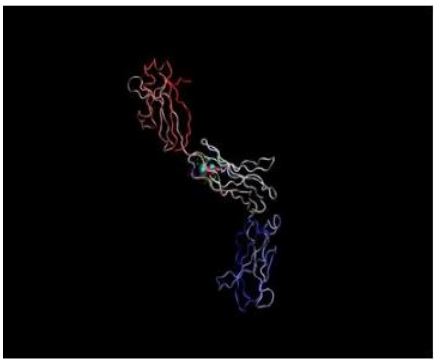
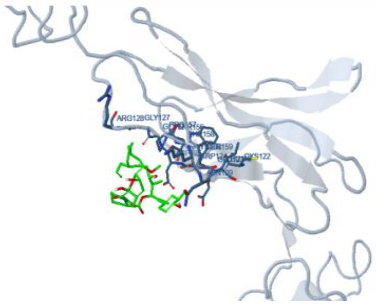
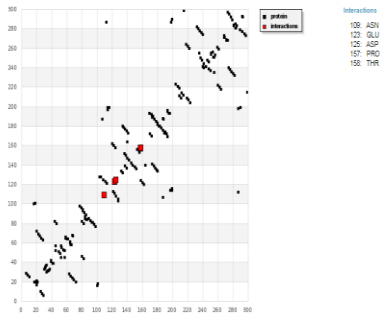
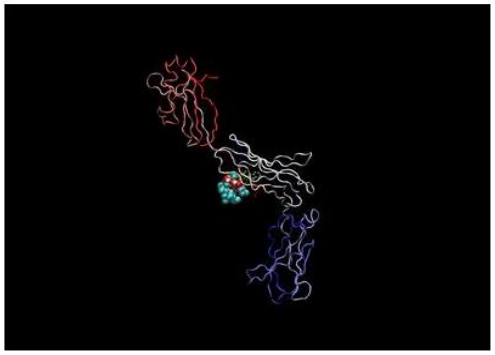
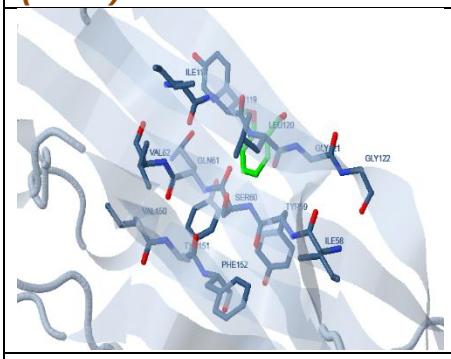
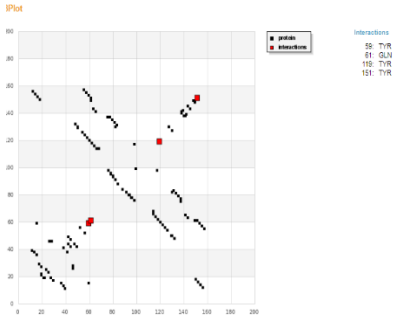
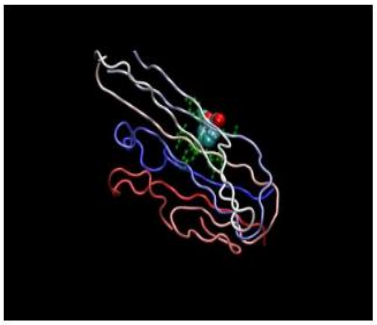
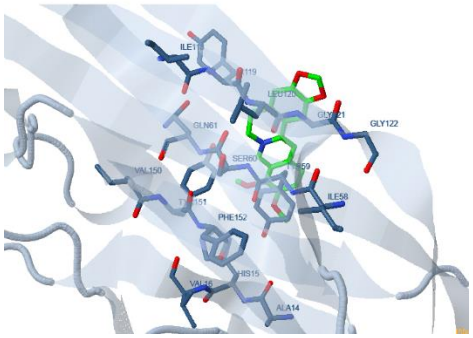
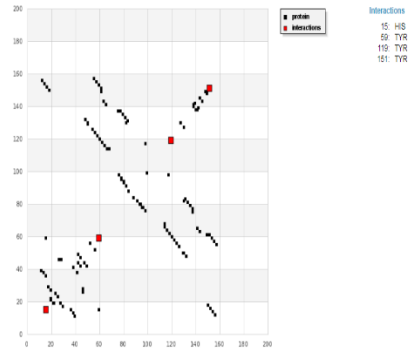
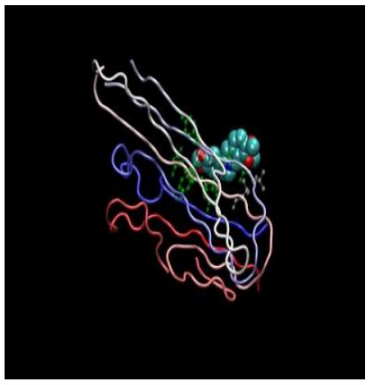
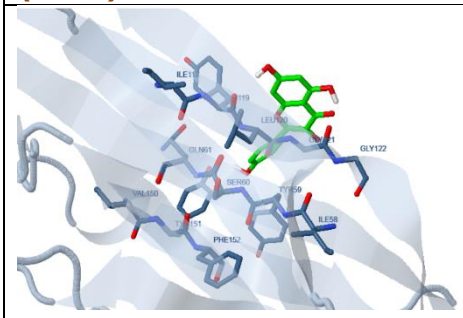
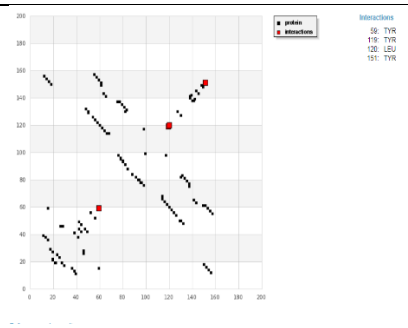
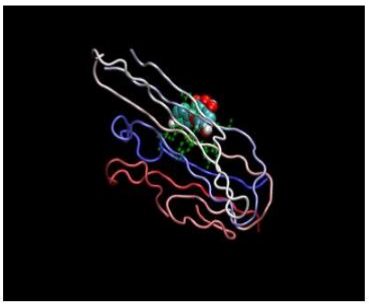
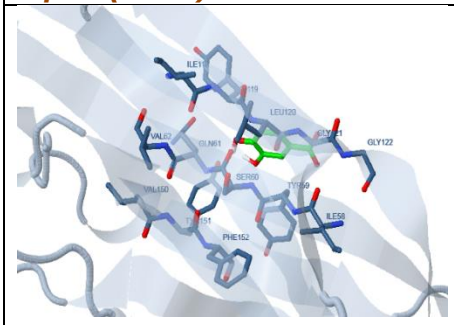
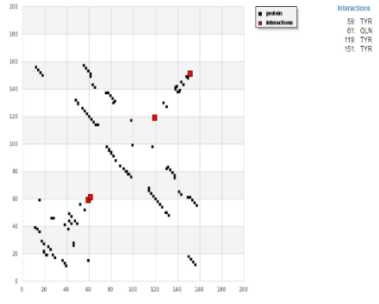
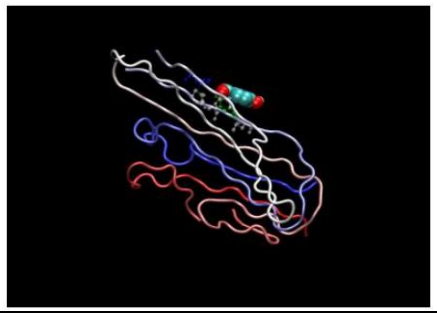
Nimbolide with IL- 6 – PDB 1P9M	HB Plotting Analysis	Receptor Ligand Complex
		
Picein with IL- 6 – PDB 1P9M	**HB Plotting Analysis**	**Receptor Ligand Complex**
		
Tacrolimus with IL- 6 – PDB 1P9M	**HB Plotting Analysis**	**Receptor Ligand Complex**
		

Figure.5.18.FINAL DOCKING REPORT TNF - α :

Anisaldehyde with TNF-alpha (2AZ5)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Berberine with TNF-alpha (2AZ5)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Kaempferol with TNF-alpha (2AZ5)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Protocatechuic acid with TNF-alpha (2AZ5)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		

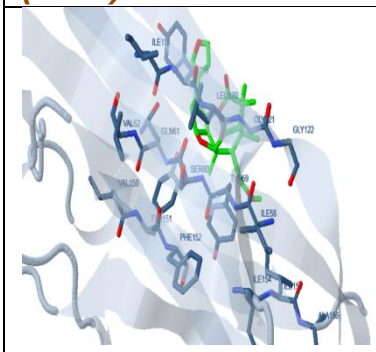
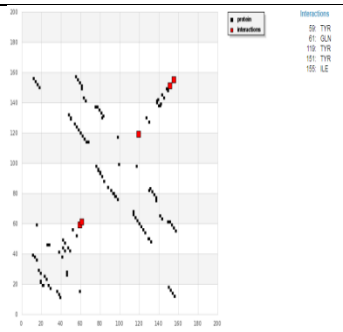
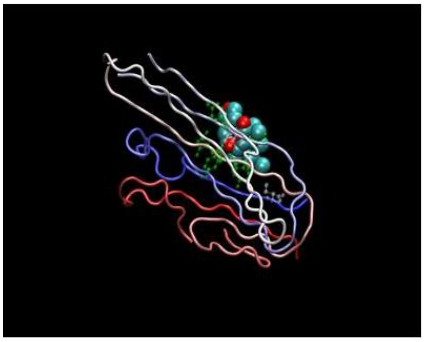
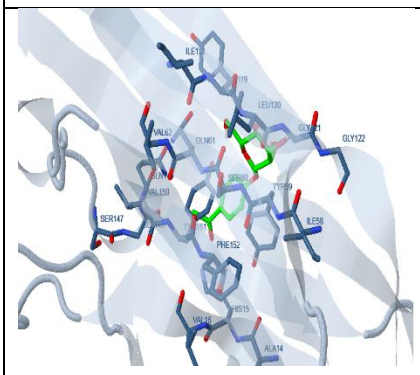
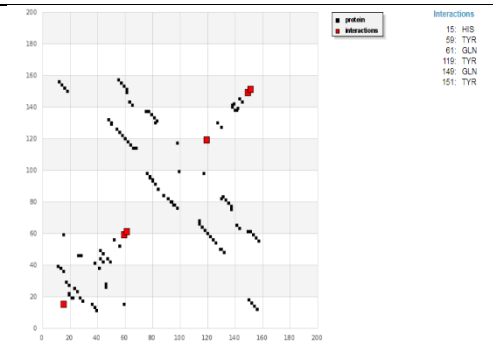
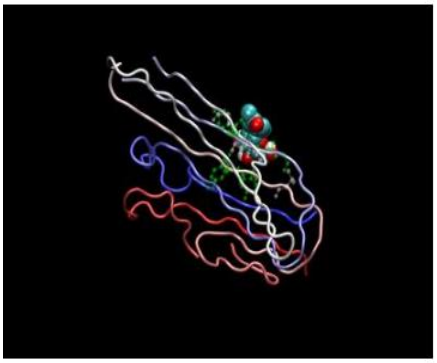
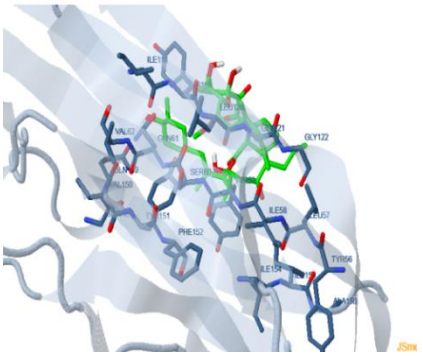
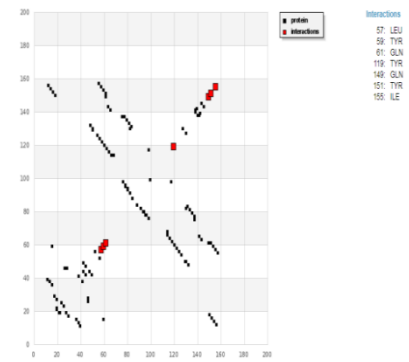
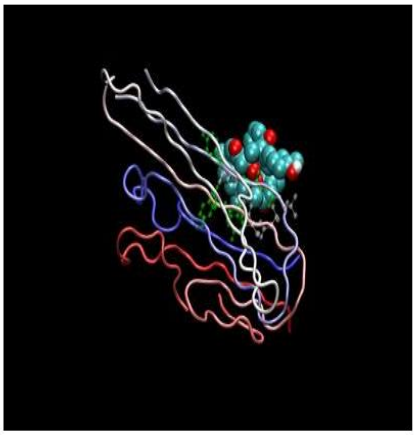
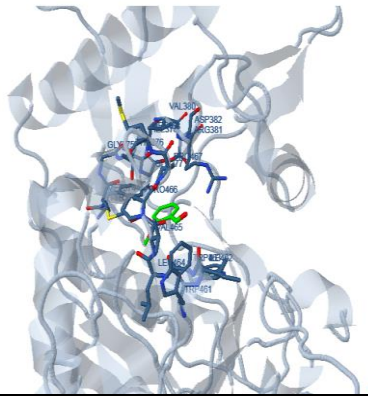
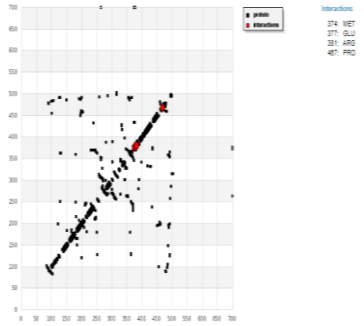
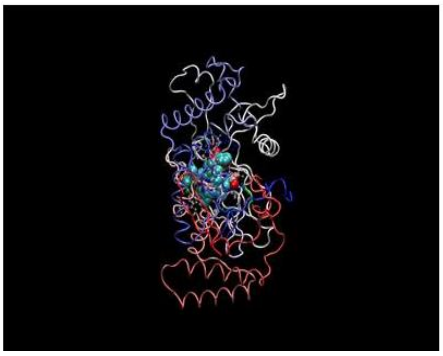
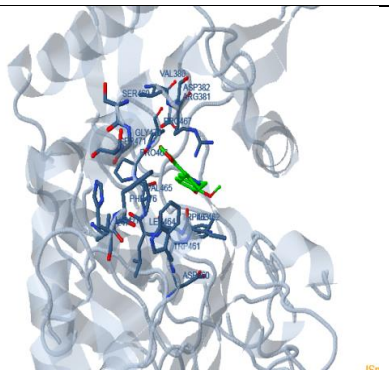
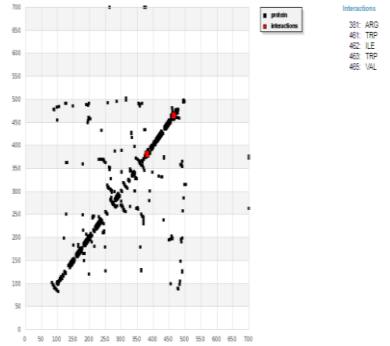
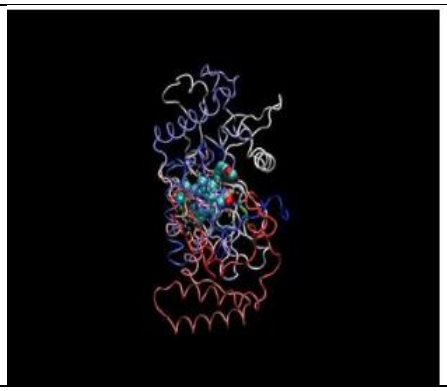
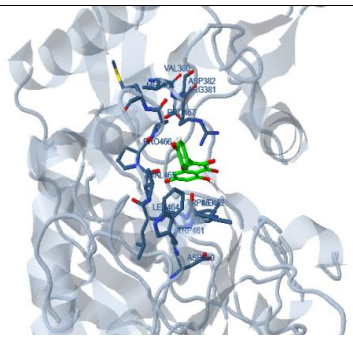
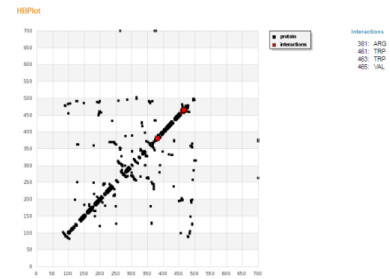
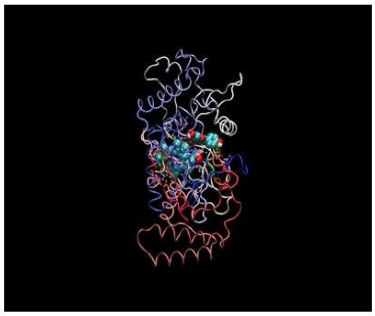
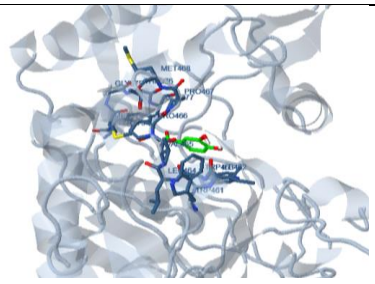
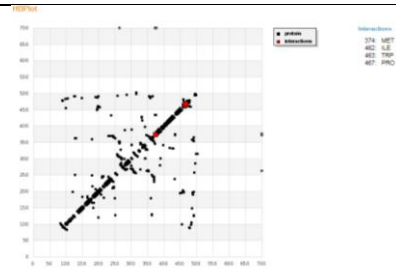
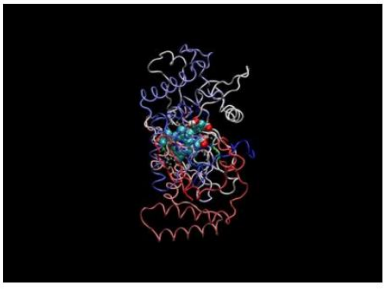
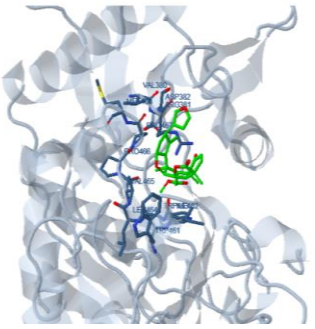
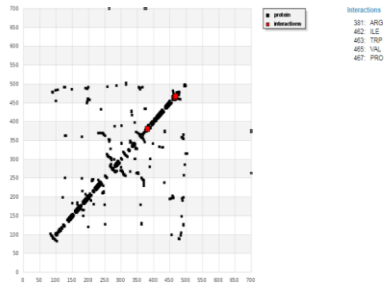
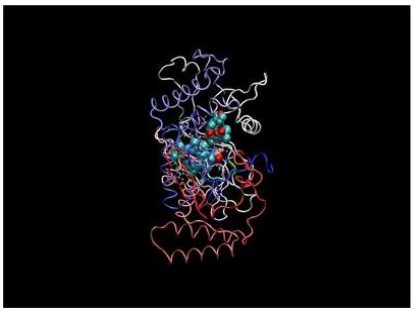
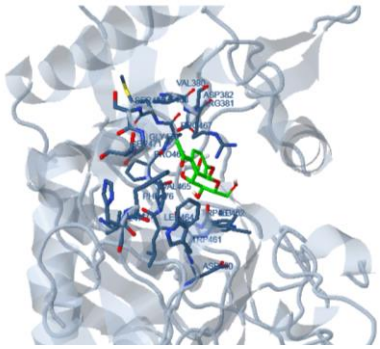
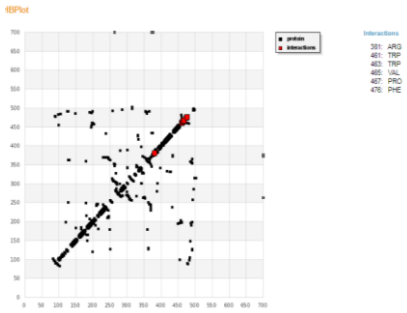
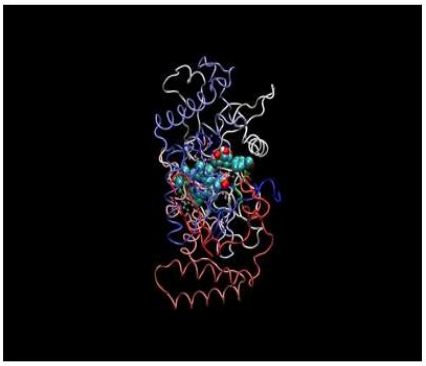
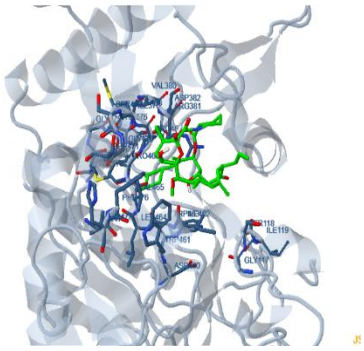
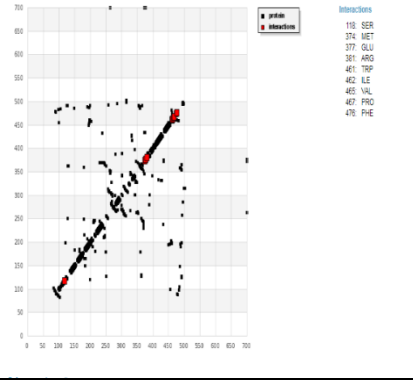
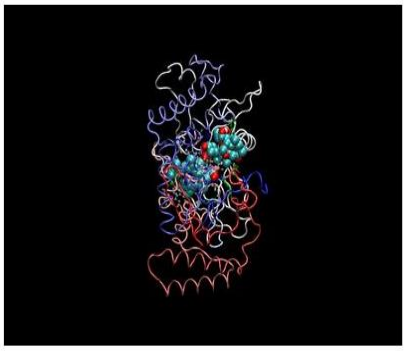
Nimbolide with TNF-alpha (2AZ5)	HB Plotting Analysis	Receptor Ligand Complex
		
Picein with TNF-alpha (2AZ5)	**HB Plotting Analysis**	**Receptor Ligand Complex**
		
Tacrolimus with TNF-alpha (2AZ5)	**HB Plotting Analysis**	**Receptor Ligand Complex**
		

Figure.5.19.FINAL DOCKING REPORT NITRIC OXIDE SYNTHASE :

Anisaldehyde with Nitric Oxide Synthase (1NSI)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Berberine with Nitric Oxide Synthase (1NSI)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Kaempferol with Nitric Oxide Synthase (1NSI)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		
Protocatechuic acid with Nitric Oxide Synthase (1NSI)	*HB Plotting Analysis*	*Receptor Ligand Complex*
		

Nimbolide with Nitric Oxide Synthase (1NSI)	HB Plotting Analysis	Receptor Ligand Complex
		
Picein with Nitric Oxide Synthase (1NSI)	**HB Plotting Analysis**	**Receptor Ligand Complex**
		
Tacrolimus with Nitric Oxide Synthase (1NSI)	**HB Plotting Analysis**	**Receptor Ligand Complex**
		

5.5.5.Sivappu Thylam :

In-vitro Anti-Inflammatory Activity by Protein (Albumin) denaturation Assay

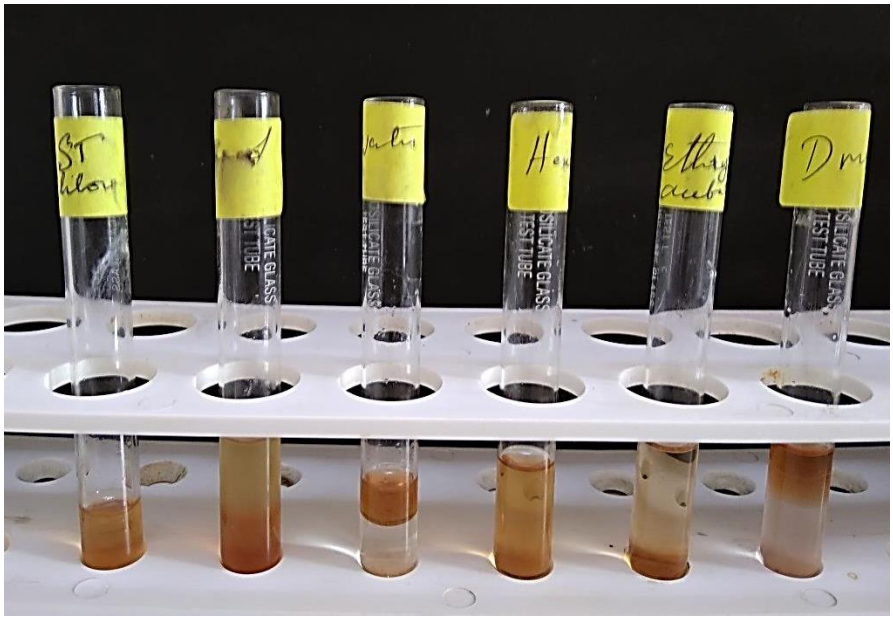


Figure.5.20.Sample Description

S.No	Solvent Used	Solubility / Dispersibility
1	Chloroform	Soluble
2	Ethanol	Insoluble
3	Water	Insoluble
4	Ethyl acetate	Soluble
5	Hexane	Soluble
6	DMSO	Insoluble

Table.5.24.Solubility Profile of ST

Sample Preparation: Chloroform Extract of the sample ST were been used for the assay

Statistical analysis

Results are expressed as Mean ± SD. The difference between experimental groups was compared by One-Way Analysis Of Variance (ANOVA) followed by Dunnet Multiple comparison test.

FINAL RESULT

Concentration in µg/ml	Percentage Inhibition of Protein Denaturation
ST 100	10.21 ± 1.45
ST 200	20 ± 1.38
ST 300	25.54 ± 0.26
ST 400	36.71 ± 2.47
ST 500	50.91 ± 0.99
Diclofenac sodium (100 µg)	97.19 ± 3.80

Table.5.25.Each value represents the mean ± SD. N=3

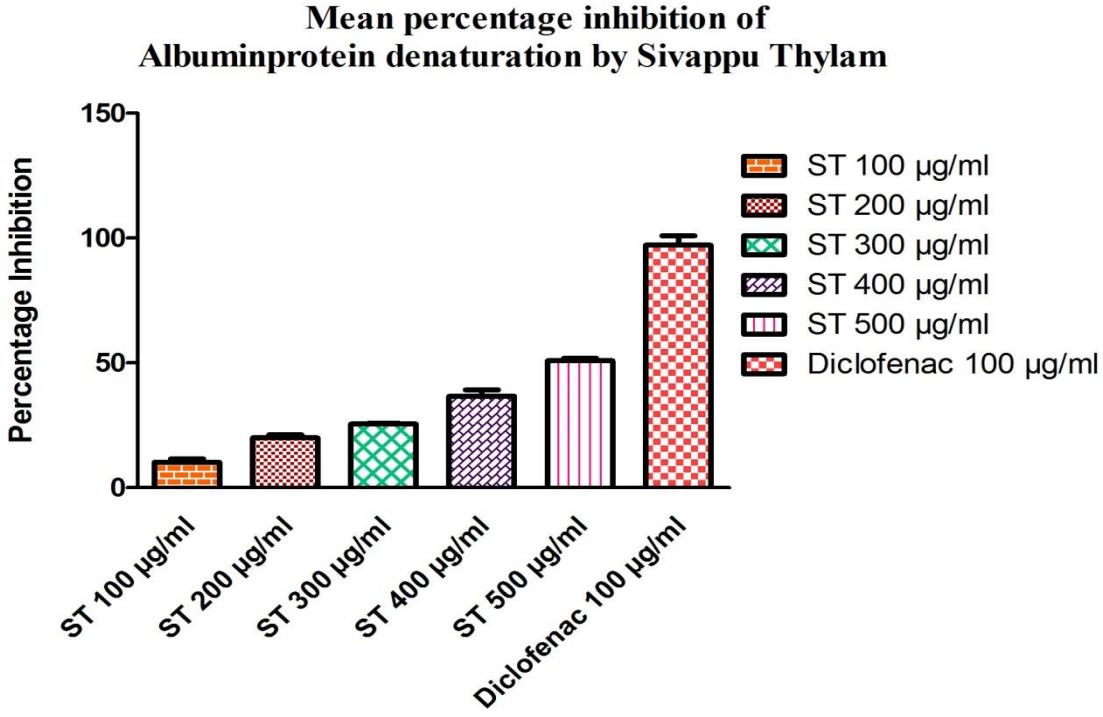


Figure.5.21.Percentage Inhibition of Protein Denaturation

Result Analysis

The result obtained from the present clearly indicates that the test drug ST was effective in inhibiting heat induced albumin denaturation. Maximum percentage inhibition of about 50.91 ± 0.99 % was observed at 500 µg/ml when compare to that of the Diclofenac sodium, a standard anti-inflammatory agent with the maximum inhibition 97.19 ± 3.80 at the concentration of 100 µg/ml.

Conclusion

From the result of the study it was concluded that the test drug ST possess promising anti-inflammatory property in protein denaturation assay.

5.6.TOXICITY STUDY

5.6.1.Acute toxicity

Parangipattai Kudineer was administered single time at the dose of 2gms/kg to rats and observed for consecutive 14 days after administration. According to the OECD guideline 423 when there is information in support of non-toxicity or low and immortality nature of the test substance, then the limit test at the dose level 2 gms/kg body weights (highest starting dose level) was conducted. All animals were observed daily once for any abnormal clinical signs. Weekly body weight and food consumption were recorded. No mortality was observed during the total period of the study. Data obtained in this study indicated no significance physical and behavioural signs of any toxicity due to administration of **Parangipattai Kudineer** at the dose of 2gms/kg to rats.

At the 14th day, all animals were observed for functional and behavioural examination. In functional and behavioural examination, home cage activity, handheld activity were observed. Home cage activities like Body position, Respiration, involuntary movement, (Clonic and Tonic), Palpebral closure, Approach response, Touch response, Pinna reflex, Sound responses, Tail pinch response were observed. Handheld activities (Reactivity and Handling), Palpebral closure, Lacrimation, Salivation, Piloerection, Papillary reflex, abdominal tone, Limb tone were observed. Functional and behavioural examination was normal in all groups. Food consumption of all treated animals was found normal as compared to control group. The results of functional and behavioural examination were elicited in (Table 5.26).

Body weight at weekly interval was measured to find out the effect of **PPK** on the growth rate. No significant body weight changes were observed between control and treatment group. There were no treatment related mortality in both control and treatment groups throughout the experimental period(Table.5.26.)

No pathological (gross) changes were observed in the experimental animals (Figure.5.23).

Table.5.26. Effect of PPK on Body weight of Wistar Rats in acute toxicity study

Treatment	Body weight (mean±SEM)		
	Day 1	Day 7	Day 14
PPK(2000mg/kg)	145± 1.674*	148.00±1.515*	151.65±1.486*

Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by dunnett's.*P*< 0.05 considered as significant by comparing treated group with control group using Graph Pad Prism 3.1. **P* > 0.05 considered as not significant.

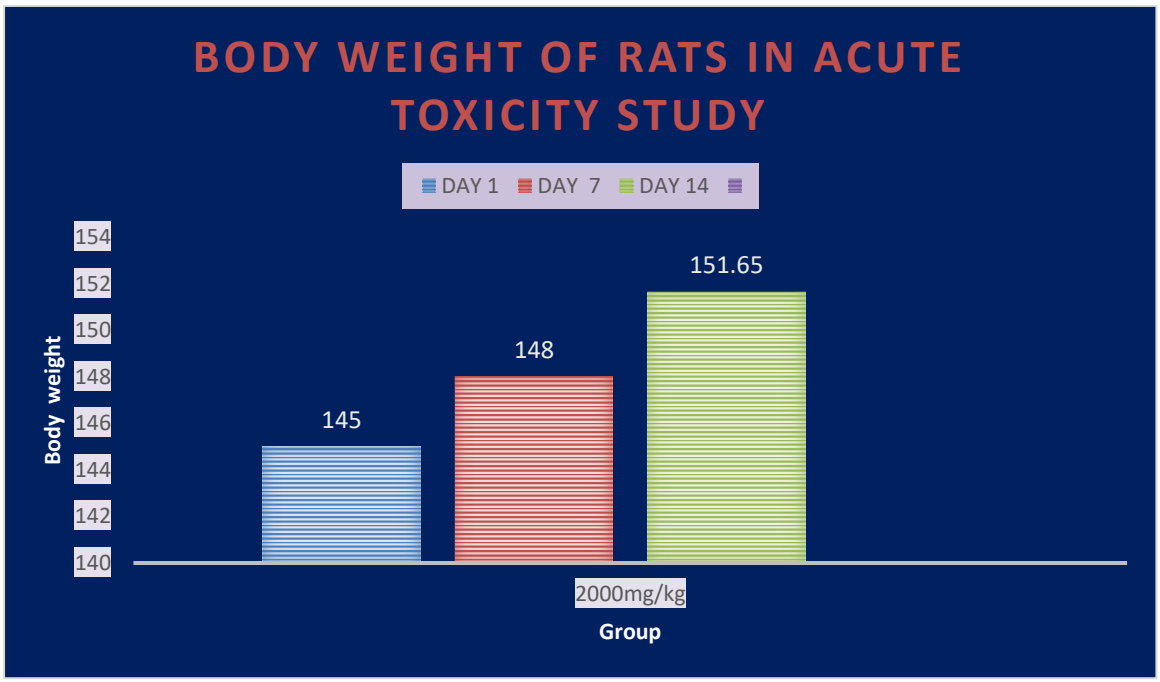


Figure.5.22.Effect of PPK on Body weight ofWistar Rats in acute toxicity study

Table.5.27. Clinical Observation of control and PPK treated experimental animals in acute toxicity study

Observations		Signs		Signs
Lethality		X	**Stereotypies (chewing)**	X
Convulsion		X	**Stereotypies (Head movements)**	X
Tremor		X	**Piloerection**	X
Straub tail		X	**Scratching**	X
Sedation	***#1***	X	**Respiration**	X
	#2	X	**Aggressiveness**	X
	#3	X	**Fear**	X
Excitation	***#1***	X	**Reactivity to touch**	X
	#2	X	**Muscle tone**	X
	#3	X	**Analgesia**	X
Abnormal gait (rolling)		X	**Ptosis**	X
Abnormal gait (tiptoe)		X	**Exophthalmos**	X
Jumps		X	**Loss of grasping**	X
Motor coordination		X	**Akinesia**	X
Loss of balance		X	**Catalepsy**	X
Fore paw treading		X	**Loss of traction**	X
Writhes		X	**Loss of corneal reflex**	X
Head twitches		X	**Loss of righting Reflex**	X
Salivation		X	**Defecation**	X
Lacrimation		X	**Others**	X

X – no sign / √ - Present; Values are expressed as mean ± SEM (n=3)

Figure.5.23. Gross Pathology of rat in acute toxicity study

Table .5.28.Gross pathology observations of control and PPK treated experimental animals

ORGANS	OBSERVATION
Brain	No abnormal lesion observed
Eyes	No abnormal lesion observed
Lymph node	No abnormal lesion observed
Trachea	No abnormal lesion observed
Oesophagus	No abnormal lesion observed
Lungs	No abnormal lesion observed
Heart	No abnormal lesion observed
Liver, Spleen	No abnormal lesion observed
Pancreas	No abnormal lesion observed
Stomach	No abnormal lesion observed
Duodenum	No abnormal lesion observed
Small and large intestine	No abnormal lesion observed
Kidney	No abnormal lesion observed
Sex organs	No abnormal lesion observed

5.6.2.Sub-Acute toxicity

5.6.2.1.Clinical Signs

No abnormal home cage activities, behavioural responses or neurological symptoms were observed before and after the exposure of PPK.

All animals in this study were free of toxic clinical signs throughout the dosing period of 28 days. (**Table).**

5.6.2.2. Mortality:

Since examination of clinical signs plays main role in toxicological testing, mortality and morbidity were recorded two times a day throughout the study. All animals in control and in all the treated dose groups survived during the dosing period of 28 days.

5.6.2.3.Body weight:

Results of body weight determination of animals from control and different dose groups exhibited comparable body weight gain (throughout the dosing period of 28 days (Table ..).

5.6.2.4.Food and water consumption:

Feed and water consumption of PPK treated groups were found to be in significant in both the sexe when compared to control. The faecal/urinary excretion patterns were also found to be normal in PPK administered rats in comparison to the vehicle treated rats.

5.6.2.5.Relative organ Weight:

Effects of PPK on relative organ weights were shown in Table (). No statistically significant changes in the relative organ weights of brain, heart, liver, spleen, lungs, kidneys and sex organs were observed between the control and PPK treated rats.

Table.5.29.Clinical Observation of control and PPKtreated experimental animals in subacute toxicity study

Observations		Signs		Signs
Lethality		X	**Stereotypies (chewing)**	X
Convulsion		X	**Stereotypies (Head movements)**	X
Tremor		X	**Piloerection**	X
Straub tail		X	**Scratching**	X
Sedation	***#1***	X	**Respiration**	X
	#2	X	**Aggressiveness**	X
	#3	X	**Fear**	X
	#4	X		
Excitation	***#1***	X	**Reactivity to touch**	X
	#2	X	**Muscle tone**	X
	#3	X	**Analgesia**	X
	#4	X		
Abnormal gait (rolling)		X	**Ptosis**	X
Abnormal gait (tiptoe)		X	**Exophthalmos**	X
Jumps		X	**Loss of grasping**	X
Motor coordination		X	**Akinesia**	X
Loss of balance		X	**Catalepsy**	X
Fore paw treading		X	**Loss of traction**	X
Writhes		X	**Loss of corneal reflex**	X
Head twitches		X	**Loss of righting Reflex**	X
Salivation		X	**Defecation**	X
Lacrimation		X	**Others**	X

X – no sign / √ - Present; Values are expressed as mean ± SEM (n=10 (5 animals/sex)

Figure.5.24.Gross Pathology of rat in subacute toxicity study

Table5.30.Effect of Paranipattai Kudineer on Body weight of experimental Wistar rats in 28 days repeated oral toxicity study:

Treatment	Body weight (mean±SEM)				
	1st day	7th day	14th day	21st day	28th day
Control	122±4	139.75±4.17**	147.35±5.49ns	156.20±7.41ns	180.20±8.16*
9 mg PPK/kg p.o/day	137±3	149.40±3.67*	161.70±2.05**	171.55±2.21**	196.80±5.52***
18mg PPK/kg p.o/day	143±4	156.88±3.91*	163.30±4.23ns	171.55±6.09ns	188.70±10.41ns
27mg PPK/kg p.o/day	151±4	159.58±2.94ns	165.13±2.75ns	178.78±4.01*	196.50±7.67*

Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by dunnett's. ns $P>0.05$ considered as not significant, *$P< 0.05$ considered as significant, **$P< 0.01$ considered as very significant, ***$P< 0.001$ considered as extremely significant by comparing treated group with control group using Graph Pad Prism 3.1.. Animal body weight slightly increased some group as per guidline.

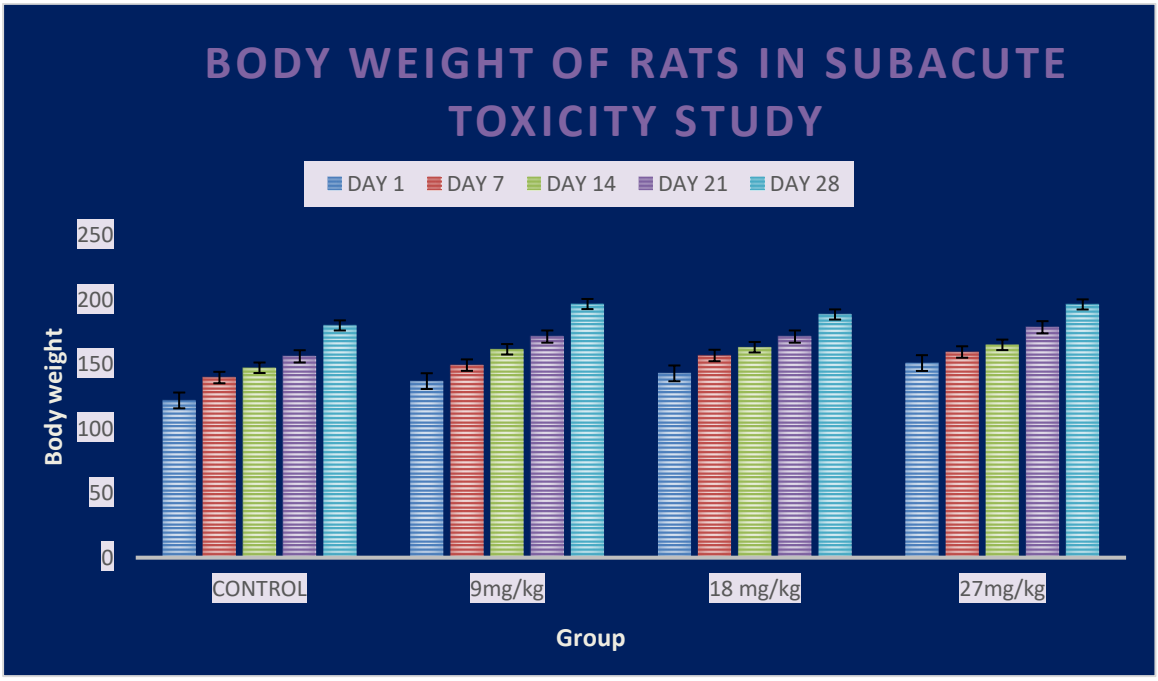


Figure 5.25. Effect of PPK on Body weight of Wistar Rats in Subacute toxicity study

Table.5.31. Effect of Paranipattai Kudineer on Organ weight of experimental Wistar rats in 28 days repeated oral toxicity study:

Group	Relative organ weight (g %) (mean±SEM)							
	Brain	Lungs	Heart	Liver	Kidney	Spleen	Sex organs	
							Testis	Ovaries
Control	1.08±0.04	0.77±0.02	0.38±0.02	3.42±0.11	0.89±0.05	0.29±0.01	0.95±0.09	0.04±0.01
9mg PPK/kg p.o/day	1.01±0.03 ns	0.73±0.03 ns	0.36±0.01 ns	3.11±0.12 ns	0.80±0.03 ns	0.30±0.01 ns	0.81±0.04 ns	0.05±0.01 ns
18mg PPK/kg p.o/day	1.07±0.06 ns	0.75±0.04 ns	0.37±0.02 ns	3.50±0.24 ns	0.86±0.05 ns	0.29±0.01 ns	0.86±0.06 ns	0.05±0.01 ns
27mg PPK/kg p.o/day	1.01±0.05 ns	0.73±0.03 ns	0.37±0.02 ns	3.30±0.18 ns	0.82±0.03 ns	0.30±0.01 ns	0.81±0.04 ns	0.04±0.01 ns

Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by dunnett's. $^{ns}P>0.05$ considered as not significant, by comparing treated group with control group using Graph Pad Prism 3.1.

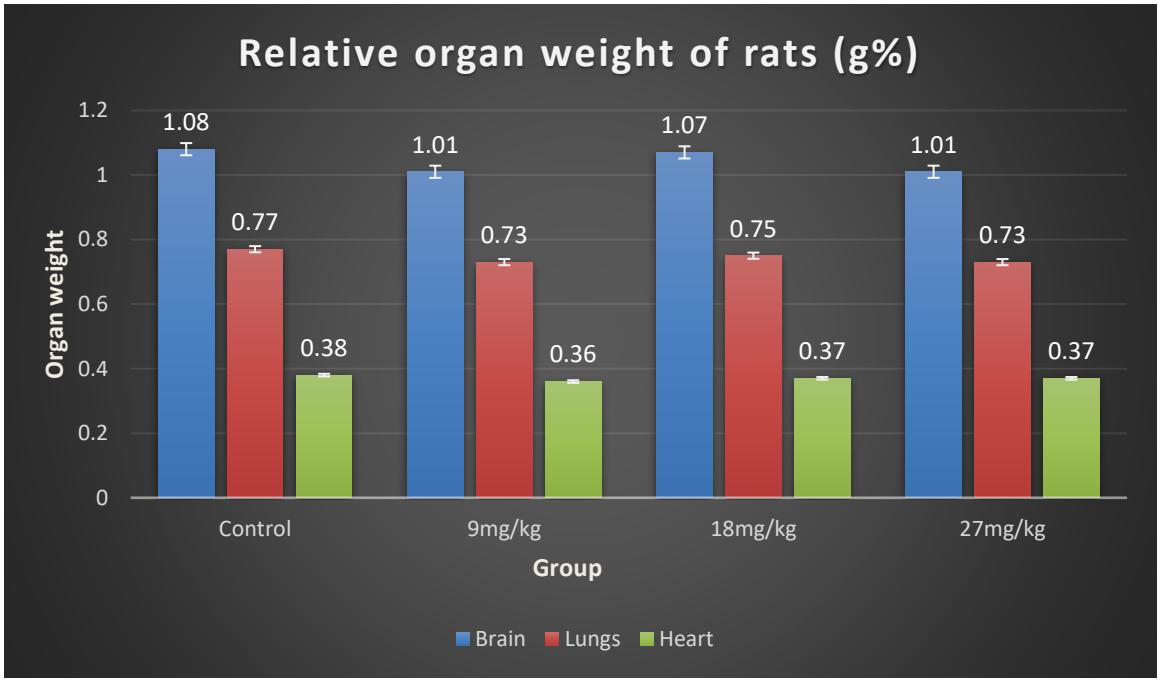


Figure5.26.Effect of PPK on relative organ weights in WA rats

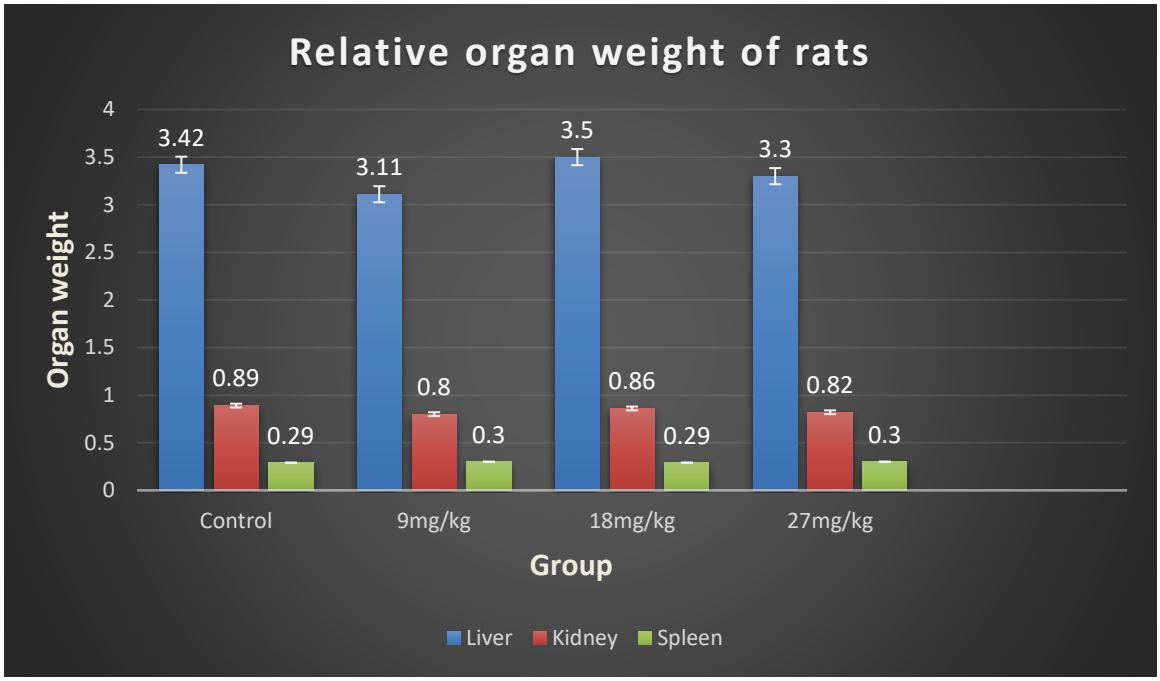


Figure.5.27. Effect of PPK on relative organ weights in WA rats

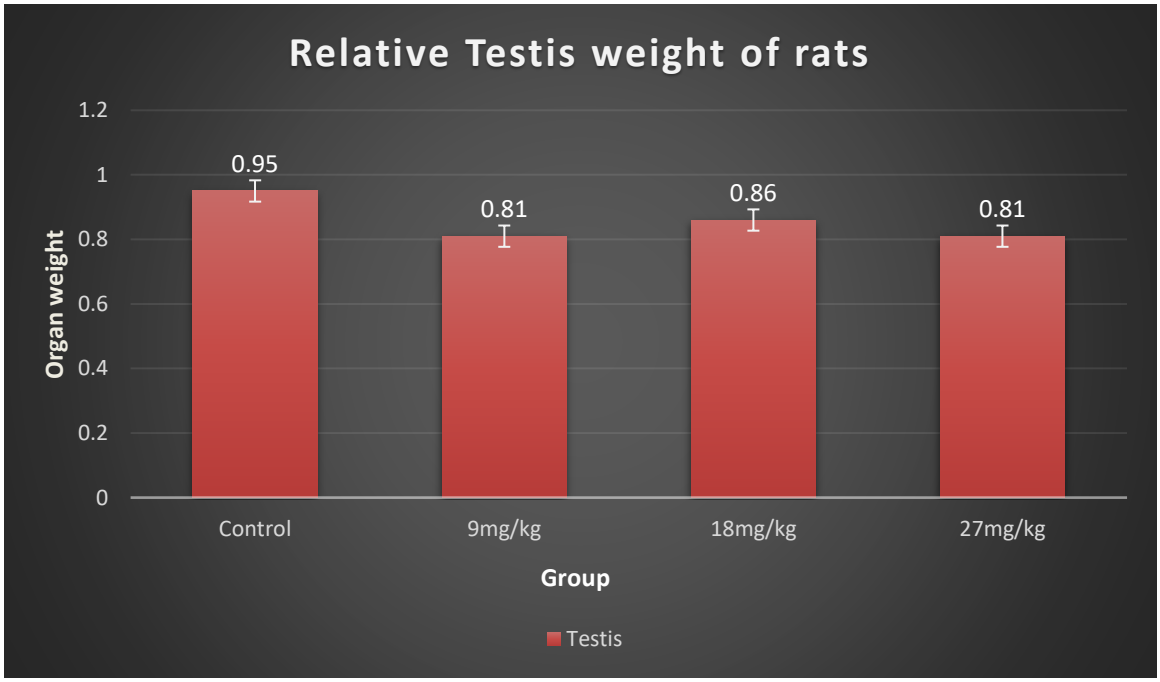


Figure.5.28.Effect of PPK on testis weight

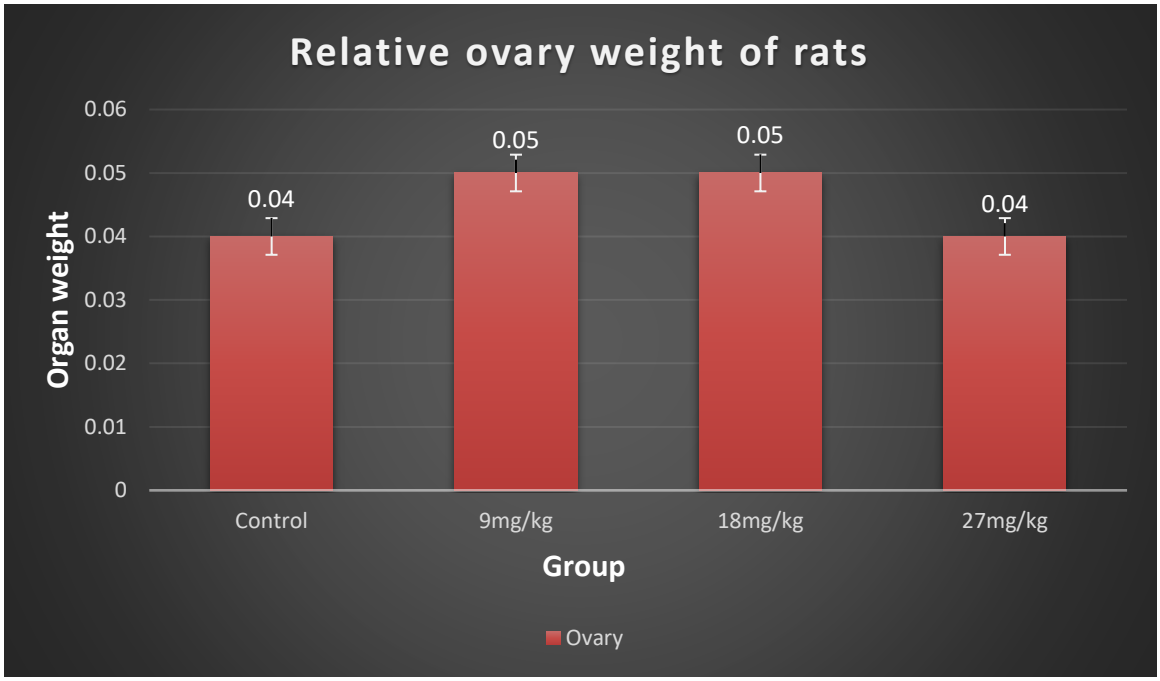


Figure.5.29.Effect of PPK on ovaries weight

5.6.2.6.Hematological investigations

The haemopoietic system serves as vital goal for toxic chemicals and is a susceptible index for pathological conditions both in humans and animals. The results of hematological investigations conducted on day 29 does not revealed any significant changes in the values of various parameters observed when compared with those of respective controls(Table 7.7.7).

5.6.2.7.Biochemical Investigations

Clinical biochemistry and hematological data holds major role in determining the toxicity induced by drugs. Transaminases (SGPT and SGOT) are good indicator of liver function and biomarkers to calculate the possible toxicity of drugs. Any elevation pertaining to these enzymes specifies their out flow into the blood stream due to injure in liver parenchymal cells. Results of Biochemical investigations conducted on days 29 does not revealed significant changes in the values of hepatic serum enzymes studied when compared with those of respective control (Table).

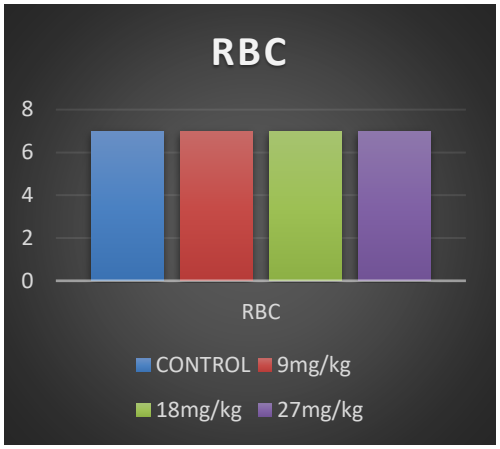
Table.5.32. Effect of Paranipattai Kudineer on Hematological Parameters of experimental Wistar rats in 28 days toxicity study:

TREATMENT	Hematological parameters(mean±SEM)										
	RBC (10^6/uL)	WBC (10^3/uL	PLT (10^3/uL	HB (g/dl)	MCH (pg)	MCV (fl)	Neutrophil (10^3/(mm^3	Eosinophil (%)	Basophil (%)	Lymphocyte (%)	Monocyte (%)
CONTROL	7±0.32	10.64± 0.44	566±22 .06	11.69± 0.28	18.57± 0.71	54.25± 1.99	2.87±0.10	1.83±0.13	0±0.00	86.61±0.50	3.28±0.09
9 mg /kg p.o/day	7±0.32	10.26± 0.91	570.60 ±17.38	11.73± 0.18	19.43± 0.44	56.65± 0.94	2.81±0.17	1.86±0.20	0.1±0.10	85.93±1.46	3.19±0.12
18 mg /kg p.o/day	7±0.32	10.76± 0.66	576±17 .13	11.81± 0.30	19.40± 0.36	57.26± 2.08	2.58±0.13	1.7±0.15	0±0.00	85±1.42	3.88±0.41
27 mg /kg p.o/day	7±0.32	10.64± 0.44	580.30 ±36.18	11.93± 0.31	19.45± 0.41	59.17± 1.00	2.58±0.19	1.74±0.19	0±0.00	85.89±1.26	3.99±0.20

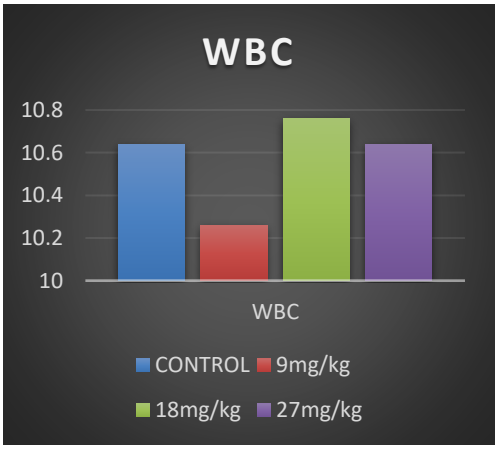
RBC: red blood corpuscles; Hb: hemoglobin; MCH: mean corpuscular hemoglobin; WBC: white blood cells PCV: packed cell volume. Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by dunnett's. *P*> 0.05 considered as not significant by comparing treated group with control group using Graph Pad Prism 3.1.

Figure 5.30. Effect of PPK over Hematological Parameters in Rats

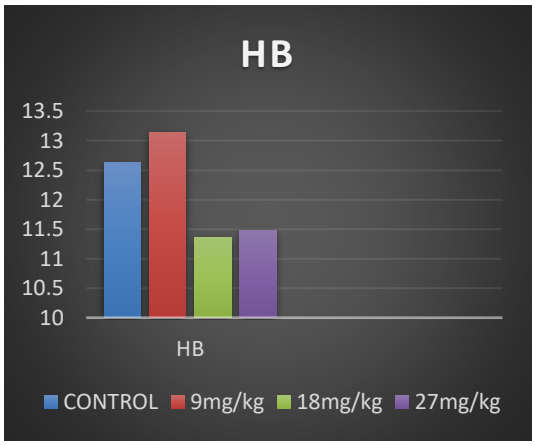
RBC Levels in PPK treated Rats



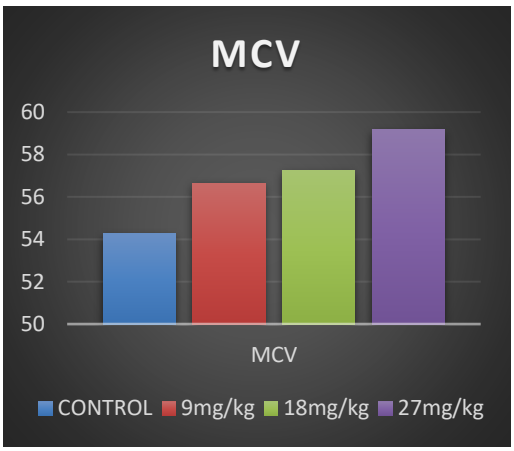
WBC Levels in PPK treated Rats



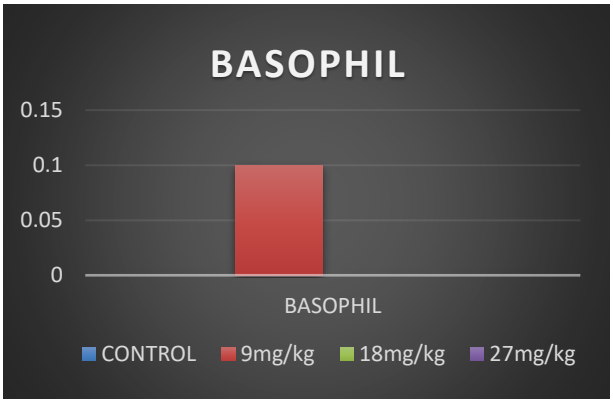
HB Levels in PPK treated Rats



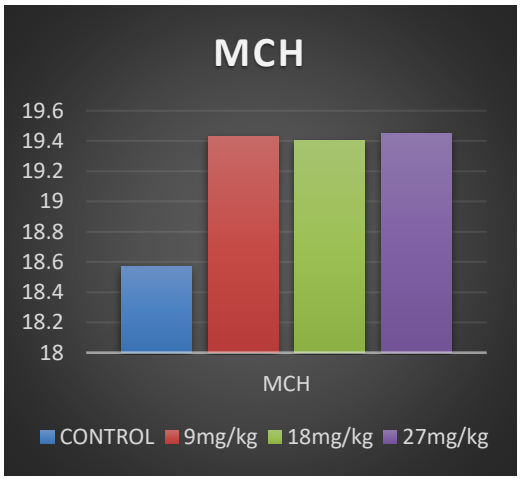
MCV Levels in PPK treated Rats



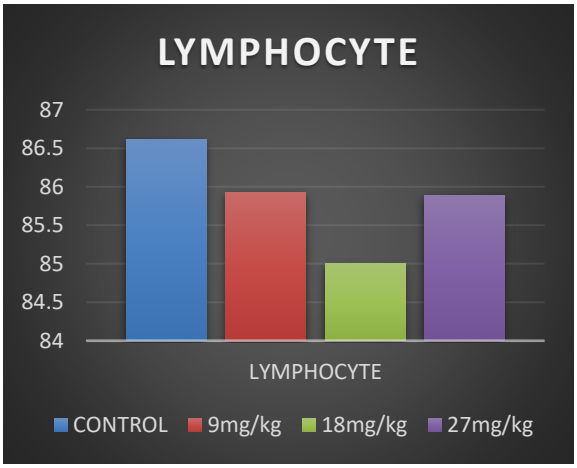
Basophil Levels in PPK treated Rats



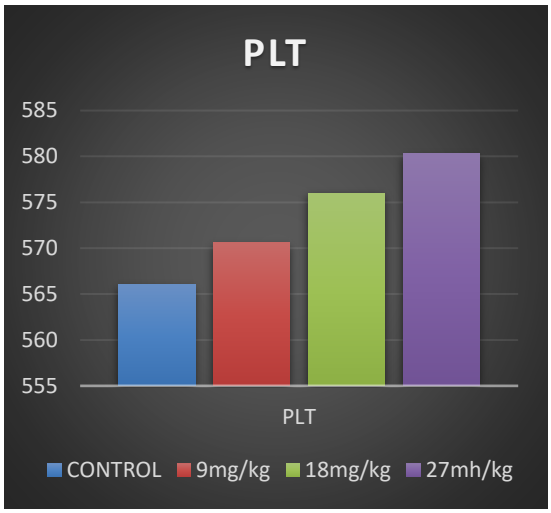
MCH Levels in PPK treated Rats



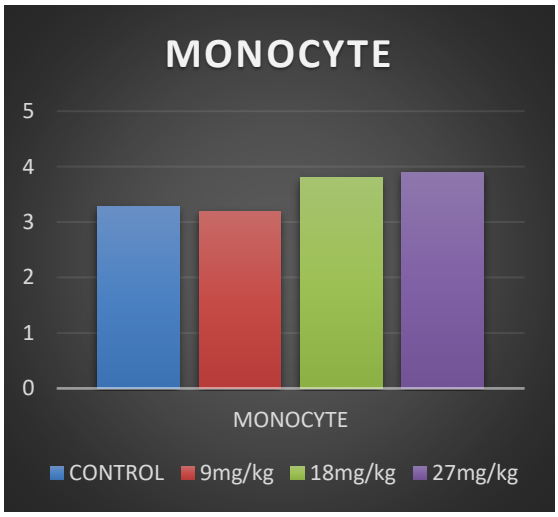
Lymphocyte Levels in PPK treated Rats



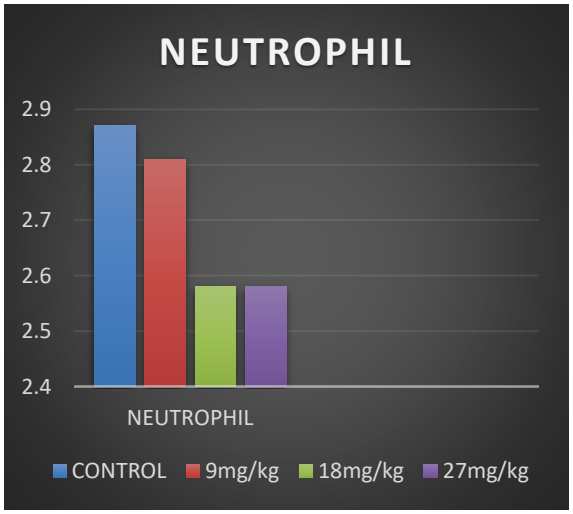
Platelet Levels in PPK treated Rats



Monocyte Levels in PPK treated Rats



Neutrophil Levels in PPK treated Rats



Eosinophil Levels in PPK treated Rats

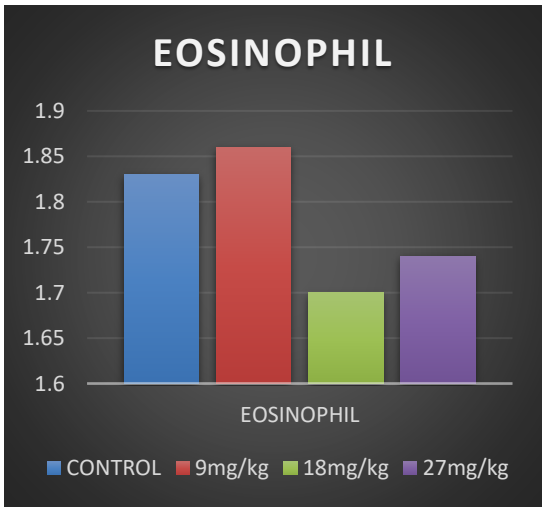


Table.5.33.Effect of Paranipattai Kudineer on biochemical parameters of experimental Wistar rats in 28 days toxicity study:

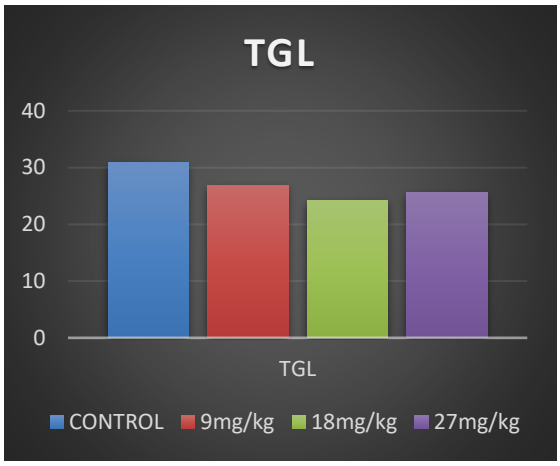
TREATMENT	Biochemical parameters(mean±SEM)									
	BUN (mg/dl)	S.Creatinine (mg/dl)	T.Bilirubin (mg/dl)	SGOT (IU/ml)	SGPT (IU/ml)	T.Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	TGL (mg/dl)
CONTROL	13±0.3162	0.86±0.10	0.86±0.16	102.25±3.47	30.62±1.96	138.59±1.14	60.38±1.57	54.9±2.50	16.59±0.81	30.83±1.71
9 mg /kg p.o/day	14±1	0.87±0.11	0.87±0.17	101.82±2.85	28.5±1.52	136.64± 3.09	56.63±1.79	48± 2.87*	15.44±0.90	26.81±1.99
18 mg /kg p.o/day	14±1	0.82±0.12	0.89±0.14	104.44±3.19	29.84±1.09	135.81±1.72	59.01±1.79	42.61±1.89	13.17±0.32	24.16±1.49
27 mg /kg p.o/day	14±1	0.83±0.14	0.83±0.14	102.16±3.20	28.6±1.61	131.57± 2.80	60.85±1.79	44.29±2.54	11.86±0.72	25.62±1.90

TGL: triglycerides, SGOT: Serum Glutamic oxaloacetic Transaminase, SGPT: serum glutamic pyruvic transaminase, ALP: Alkaline phosphatase.

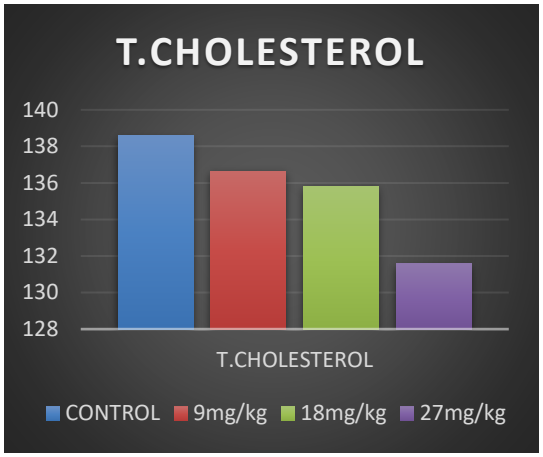
Values are expressed as mean ± SEM. Statistical significance (p) calculated by one way ANOVA followed by dunnett's. $P>0.05$ considered as not significant , $P<0.05$ considered as significant (but within normal value)by comparing treated group with control group using Graph Pad Prism 3.1.

Figur 5.31. Effect of PPK over Biochemical Parameters in Rats

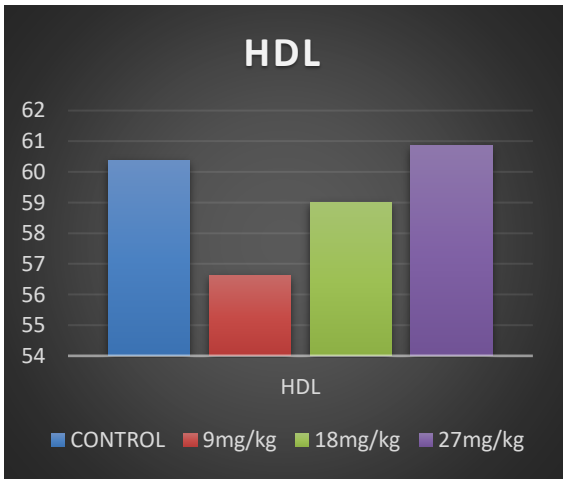
TGL Levels in PPK treated Rats



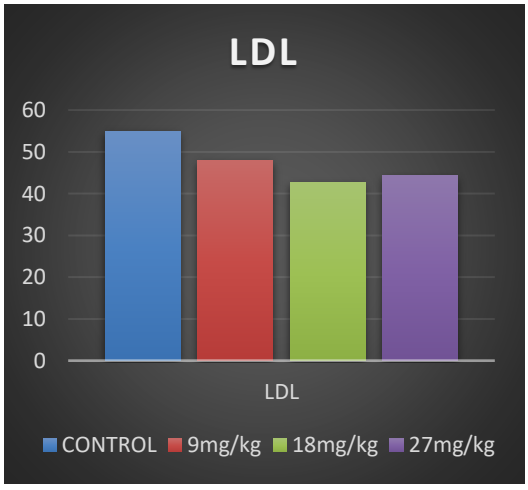
T.Cholesterol Levels in PPK treated Rats



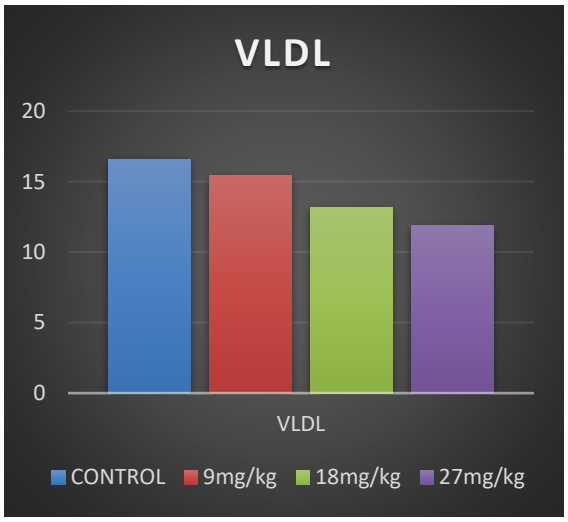
HDL Levels in PPK treated Rats



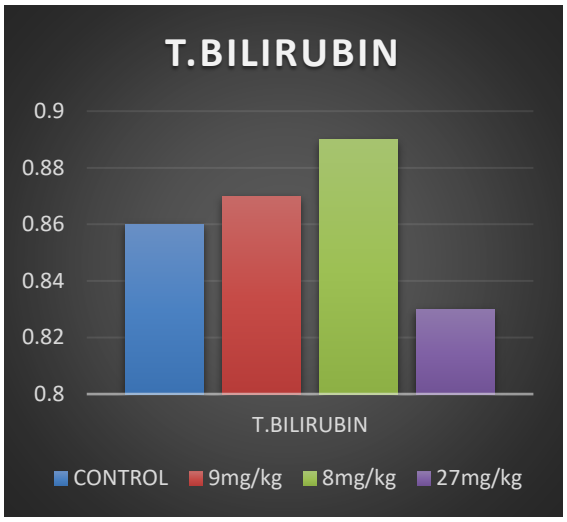
LDL Levels in PPK treated Rats



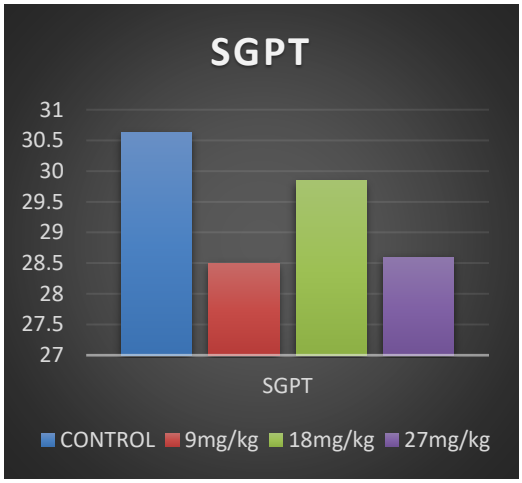
VLDL Levels in PPK treated Rats



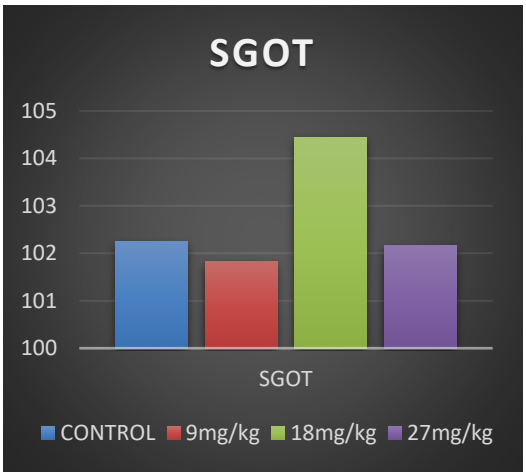
T.BILIRUBIN Levels in PPK treated Rats



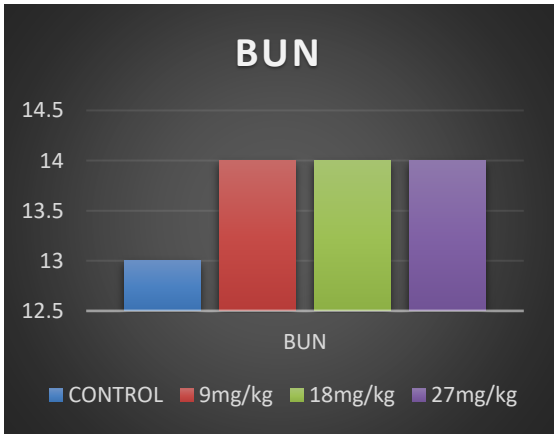
SGPT Levels in PPK treated Rats



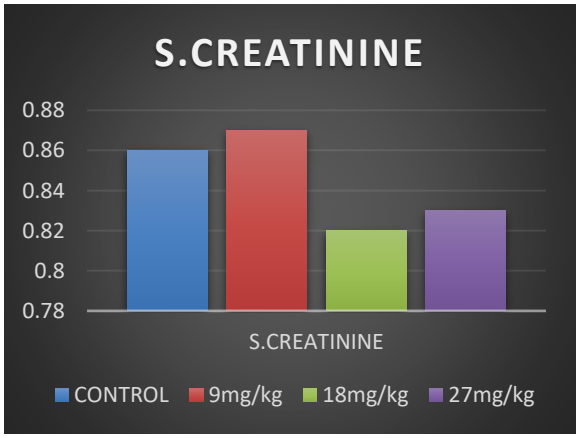
SGOT Levels in PPK treated Rats



BUN Levels in PPK treated Rats



Creatinine Levels in PPK treated Rats



5.6.2.8.Histopathology:

Histopathological studies give supportive evidence for biochemical and haematological observations. The histopathological examination carried out in the control and high dose animals treated with PPK. In histopathological examination, revealed normal architecture in comparison with control and all treated group animals (Table 7.7.9).

Table.5.34. Gross pathology observations of control and PPK treated experimental animals

ORGANS	OBSERVATION
Brain	No abnormal lesion observed
Heart	No abnormal lesion observed
Lung	No abnormal lesion observed
Stomach	No abnormal lesion observed
Liver	No abnormal lesion observed
Spleen	No abnormal lesion observed
Kidney	No abnormal lesion observed
Uterus	No abnormal lesion observed
Ovary	No abnormal lesion observed
Testes	No abnormal lesion observed

Figure 5.32. Effect of PPKon Histopathological changes in Rat organs Sub acute Toxicity study

SPECIMEN
BRAIN

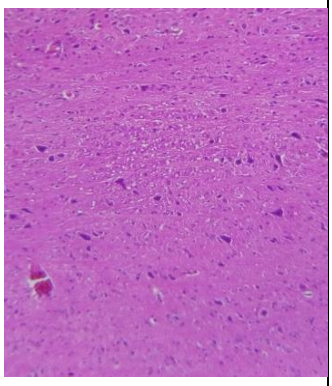
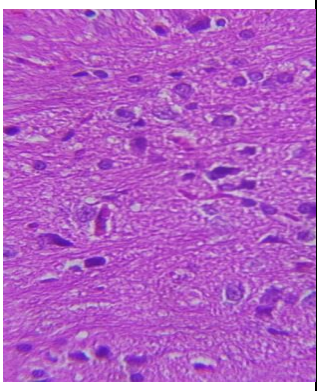
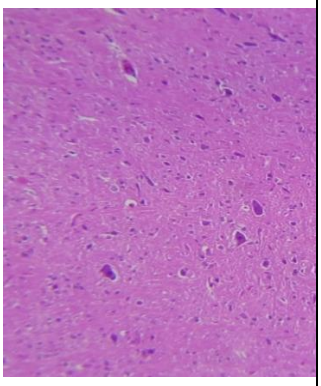
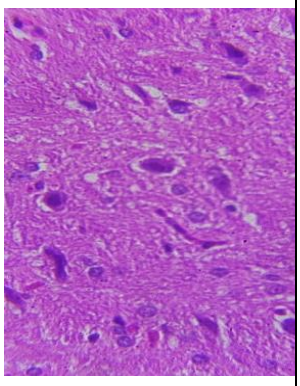
Brain Control 10x	Brain Control 40x	Brain High dose 10x	Brain High dose 40x
			

Plate: Effect of PPK on Brain in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN
HEART

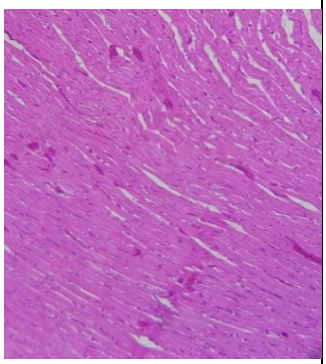
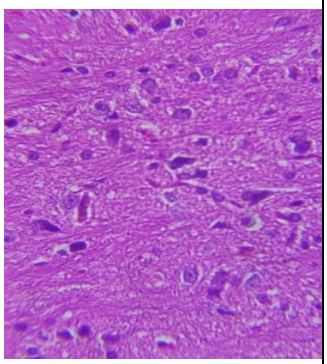
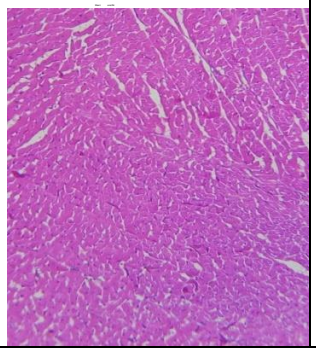
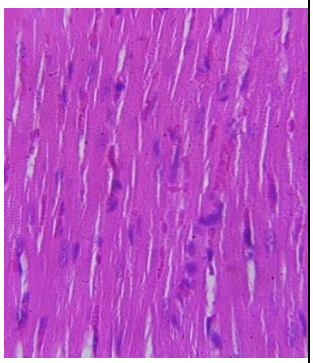
Heart Control 10x	Heart Control 40x	Heart High dose 10x	Heart High dose 40x
			

Plate: Effect of PPK on Heart in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

LUNGS

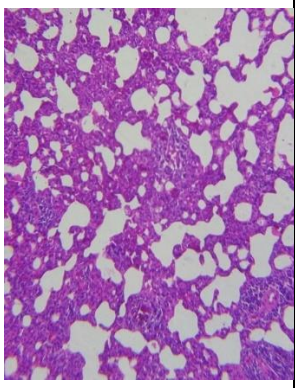
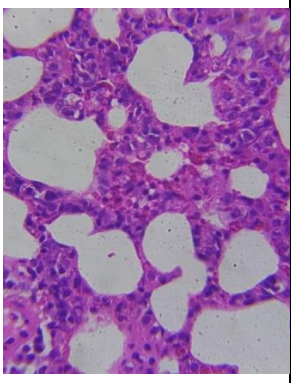
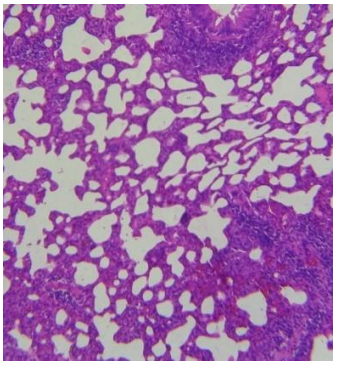
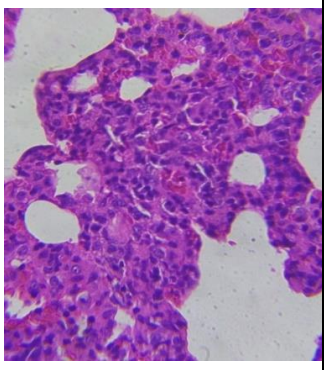
Lungs Control 10x	Lungs control 40x	Lungs High dose 10x	Lungs High dose 40x
			

Plate: Effect of PPK on Lungs in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

STOMACH

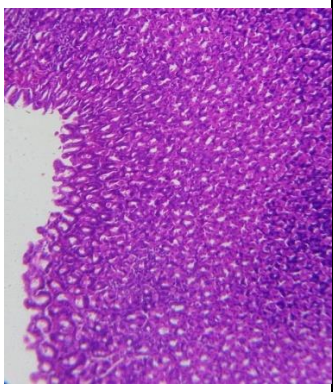
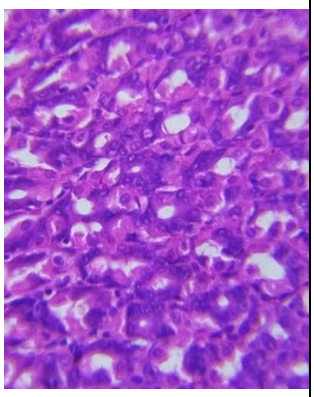
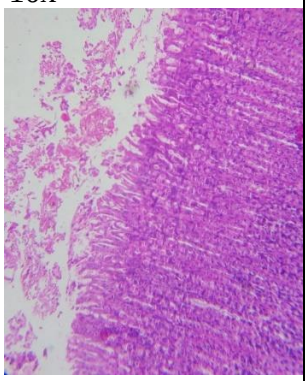
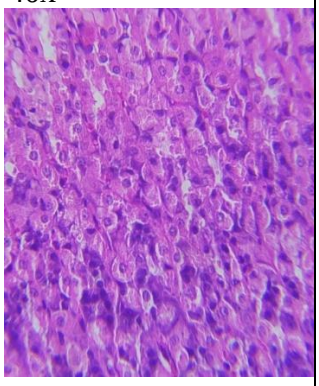
Stomach Control 10x	Stomach control 40x	Stomach High dose 10x	Stomach High dose 40x
			

Plate: Effect of PPK on Stomach in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

LIVER

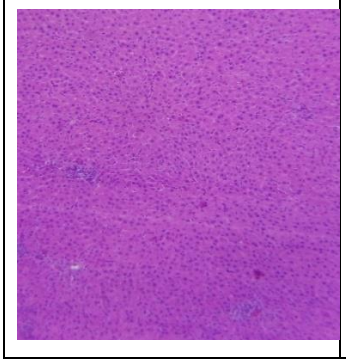
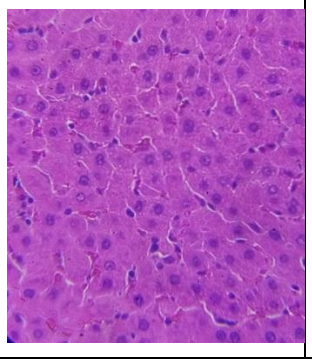
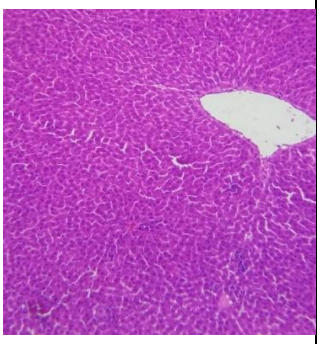
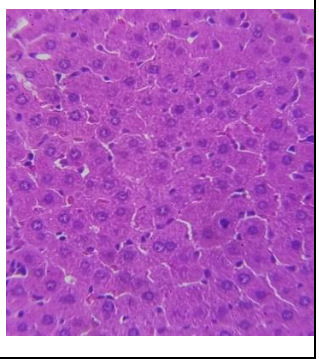
Liver Control 10x	Liver Control 40x	Liver High dose 10x	Liver High dose 40x
			

Plate: Effect of PPKon Liver in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

SPLEEN

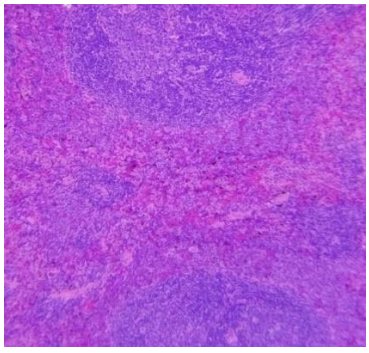
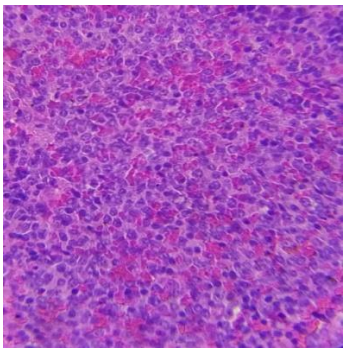
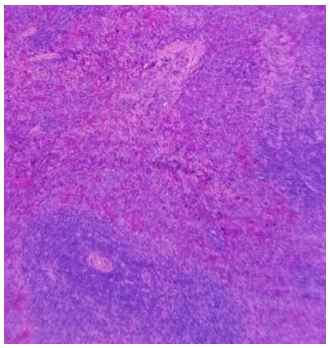
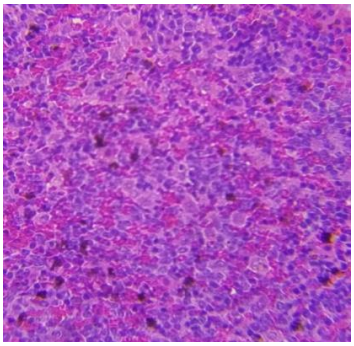
Spleen Control 10x	Spleen Control 40x	Spleen High dose 10x	Spleen High dose 40x
			

Plate: Effect of PPK on Spleen in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

KIDNEYS

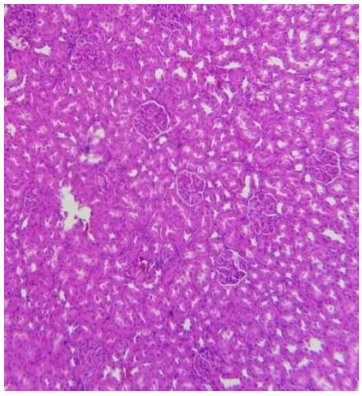
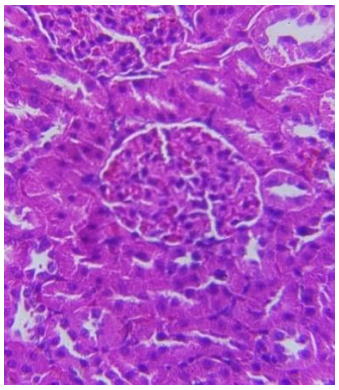
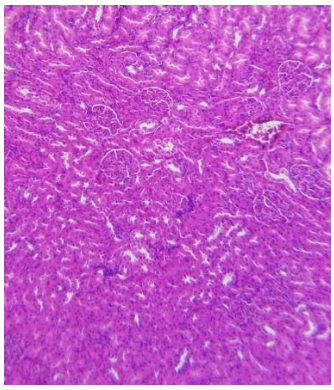
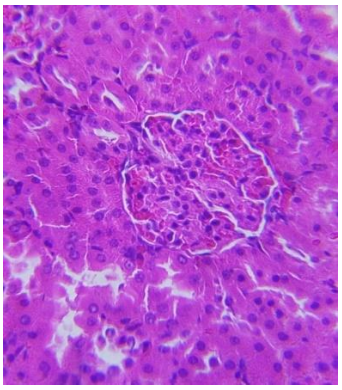
Kidneys Control 10x	Kidneys Control 40x	Kidneys High dose 10x	Kidneys High dose 40x
			

Plate: Effect of PPKon Kidneys in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

UTERUS

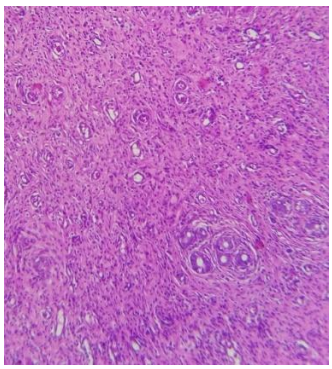
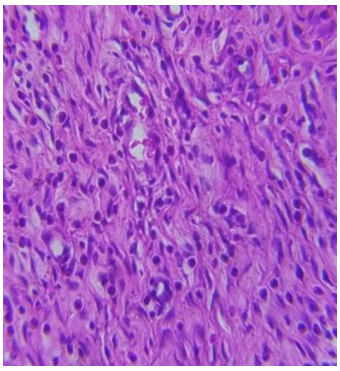
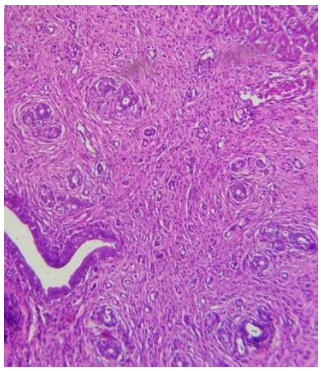
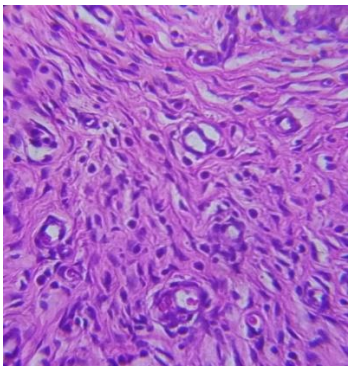
Uterus Control 10x	Uterus Control 40x	Uterus High dose 10x	Uterus High dose 40x
			

Plate: Effect of PPK on Uterus in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

OVARY

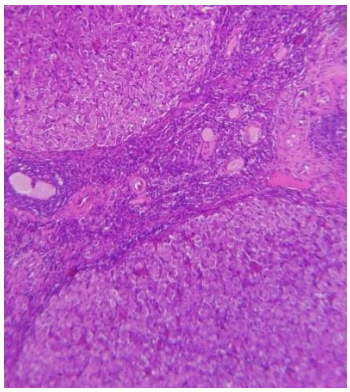
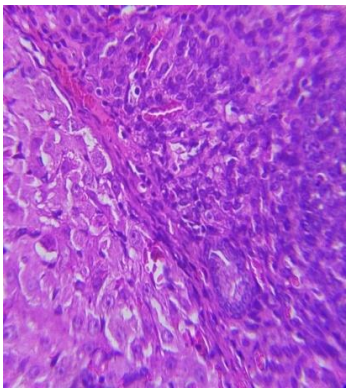
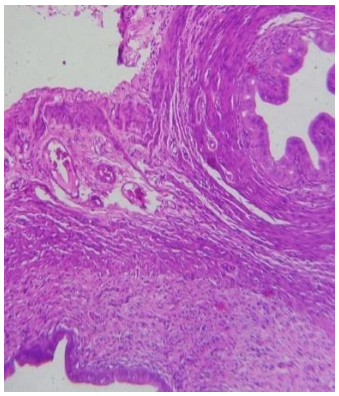
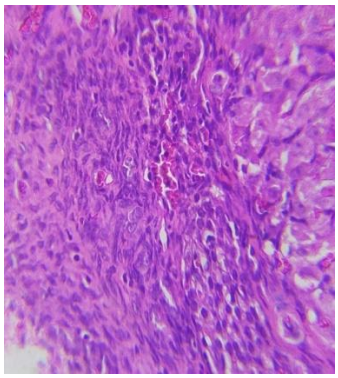
Ovary Control 10x	Ovary Control 40x	Ovary High dose 10x	Ovary High dose 40x
			

Plate: Effect of PPK on Ovary in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

SPECIMEN

TESTIS

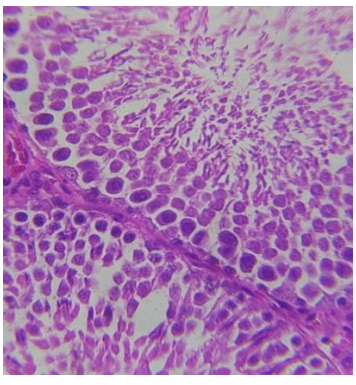
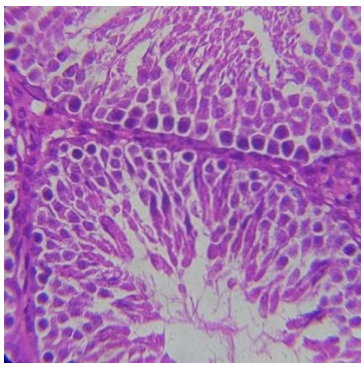
Testis Control 10x	Testis Control 40x	Testis High dose 10x	Testis High dose 40x
			

Plate: Effect of PPK on Testis in Wistar albino rats - 28 day repeated oral toxicity study.

Group	Impression
Control	No changes
High dose	No changes

5.7.Clinical study:

118 subjects were screened for Psoriasis at National Institute of Siddha. Subjects those fulfilled the inclusion criteria were recruited after obtaining informed consent. Totally 43 numbers of Kalanjagapadai (Psoriasis) individuals of both genders were recruited in this study. 3 patients had withdrawn from the study. 40 patients had completed the entire course of trial period.

Number of patients screened for eligibility: 118

Number of patients included in trial: 43

Number of patients withdrawn from the trial: 3

Number of patients who reported adverse drug reactions: 0

Duration of trial: 48 days (Treatment period)

5.7.1.Gender distribution:

S.NO	Sex	No of Cases	Percentage
1.	Male	30	75%
2.	Female	10	25%

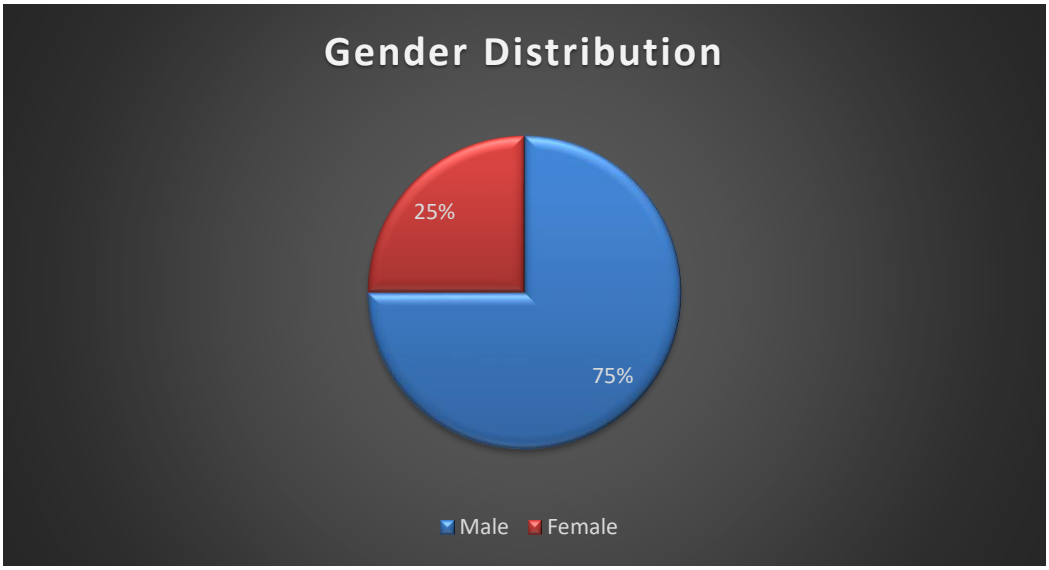


Figure5.7.1. Gender distribution

Observation:

Among the 40 patients selected for this study, 75% were males and 25% females.

5.7.2. Distribution of age interval :

Sl. No	Age	No of Cases	Percentage
1	18-30	11	27.5%
2	31-40	10	25%
3	41-50	10	25%
4	51-60	9	22.5%

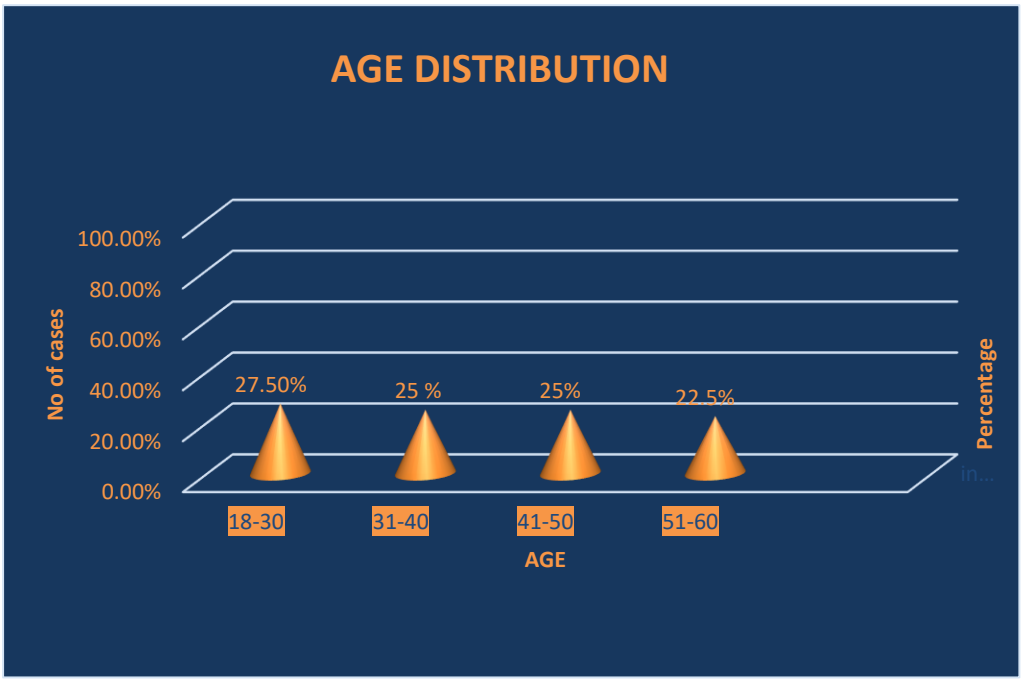


Figure5.7.2. Distribution of age interval

Observation:

The patients selected were from all age groups as given above and the maximum numbers of patients were in the age between 18 and 30.

5.7.3. Kaalam Distribution (According to Age):

Sl No	Kaalam	No of Cases	Percentage
1	Vaatha Kaalam (1-33 Years)	15	37.5%
2	Pitha Kaalam (34-66 years)	25	62.5%
3	Kaba Kaalam (67-100 years)	0	0%

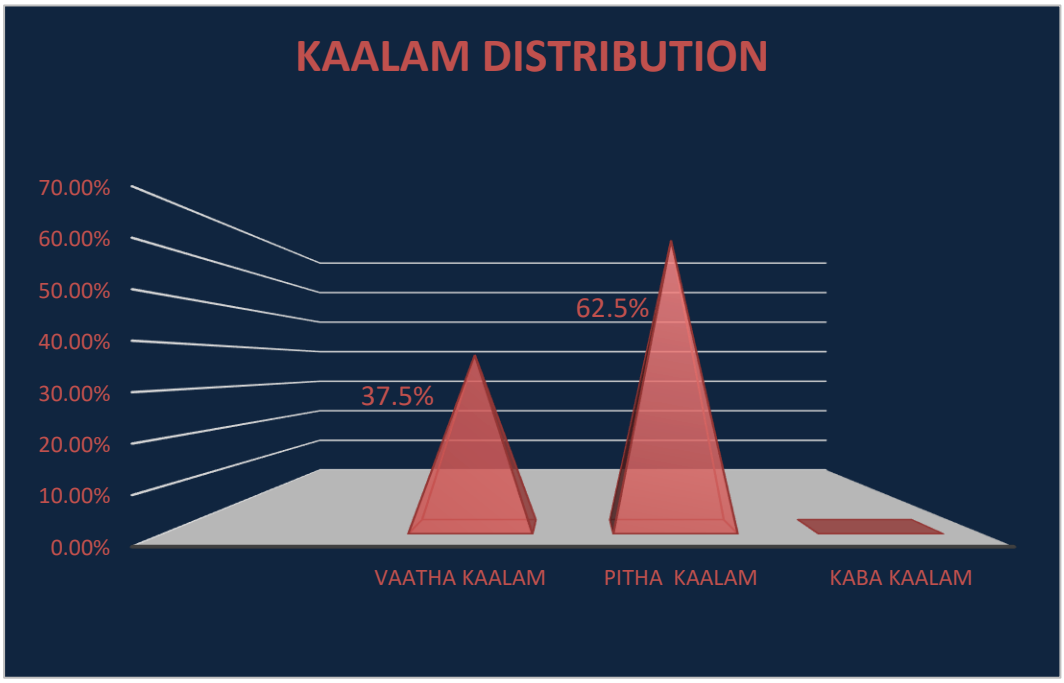


Figure. 5.7.3. Kaalam Distribution

Observation:

Out of 40 patients, 15 in Vaatha kaalam and the remaining 25 patients reported in Pitha kaalam.

5.7.4. Distribution of the occupation of the trial subjects:

S. No	Occupation	No of Cases	Percentage
1	Homemaker	4	10 %
2	Student	1	2.5 %
3	Field work with intellectual job	7	17.5 %
4	Field work with physical exertion	28	70 %

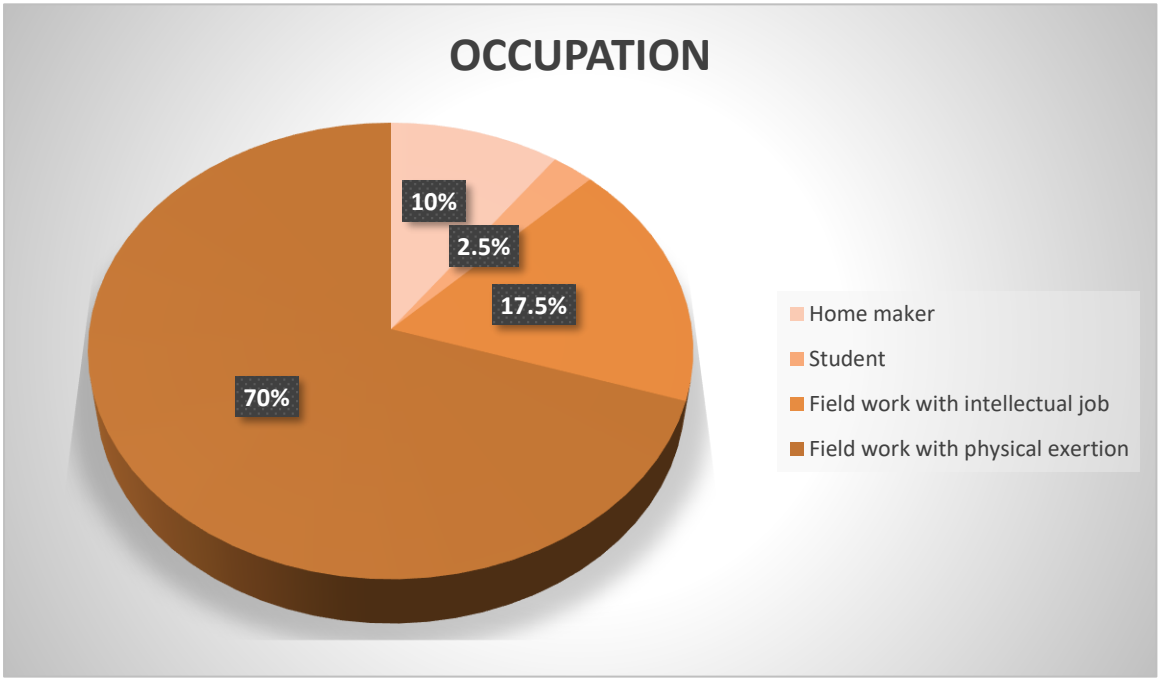


Figure. 5.7.4. Distribution of the occupation of the trial subjects

Observation:

The majority of patients in this study were Field work with physical exertion(70%).

5.7.5. Family History :

Sl. No	Criteria	No of Cases	Percentage
1	Family History (+ve)	6	15 %
2	Family History (-ve)	34	85 %

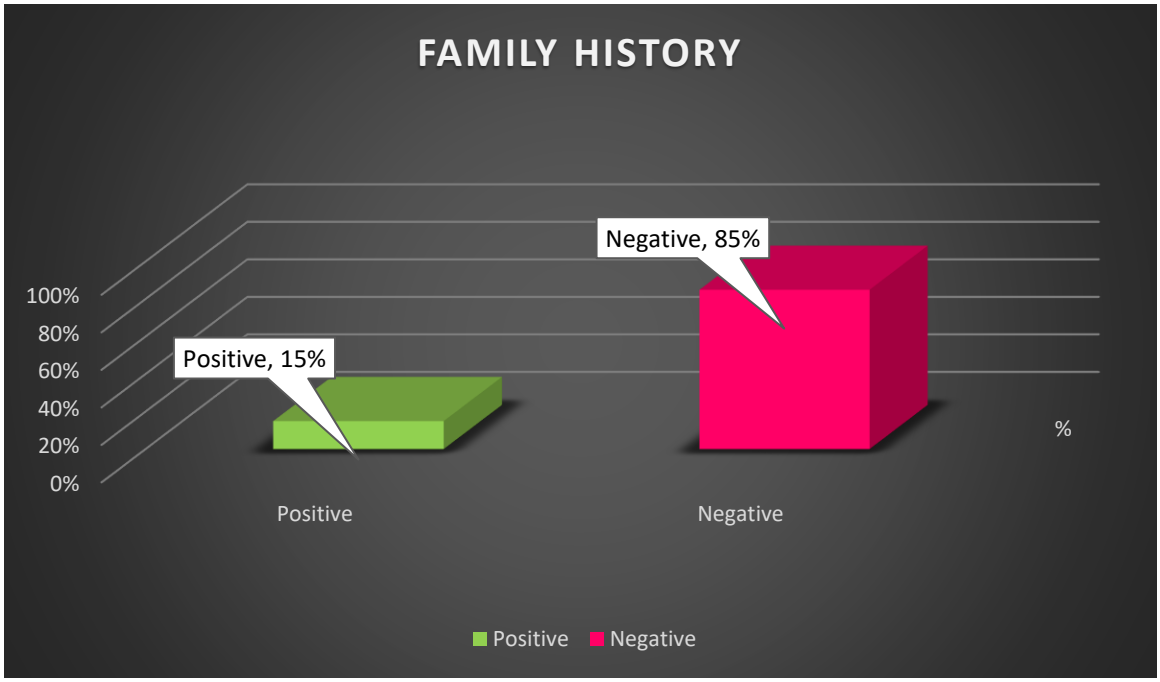


Figure5.7.5. Family History

Observation:

85 % of the patients showed negative family history.

5.7.6.History of Remissions and Relapses:

Sl. No	Remissions and relapses	No of Cases	Percentage
1	Present	36	90 %
2	Absent	4	10 %

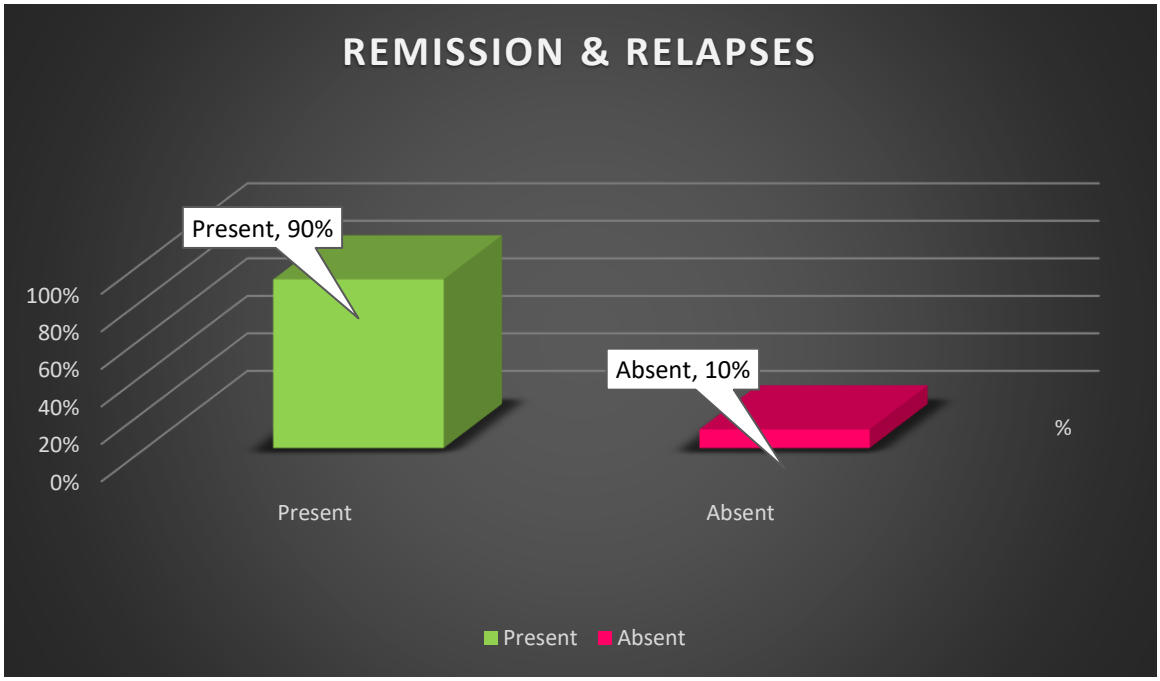


Figure 5.7.6.History of Remissions and Relapses

Observation:

90% of patients had the previous history of remission and relapse.

5.7.7. Diet habits of the trial participants:

Sl. No	Dietary Habits	No of Cases	Percentage
1	Vegetarian	6	15 %
2	Non Vegetarian	34	85 %

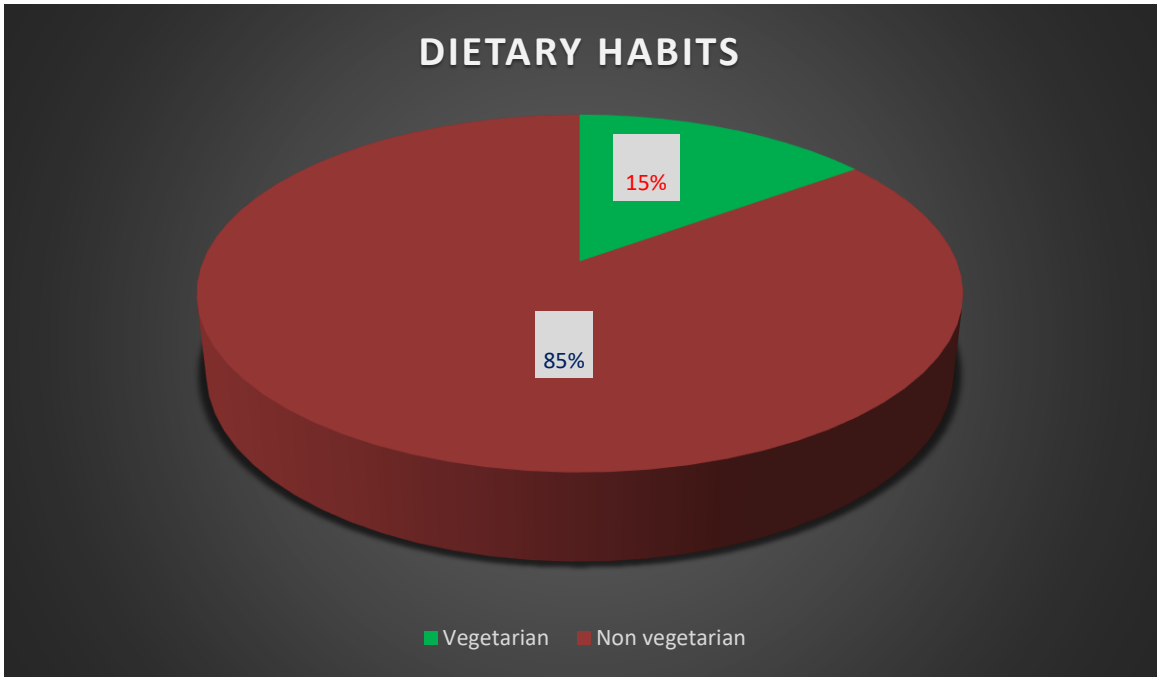


Figure 5.7.7 Diet habits of the trial participants

Observation:

85 % cases were non-vegetarians.

5.7.8. Distribution of habits in the study participants:

S.No	Habits	No of Cases	Percentage
1	Smoking	0	0 %
2	Tobacco	3	7.5 %
3	Alcohol	4	10 %
4	Smoking and Alcohol	6	15 %

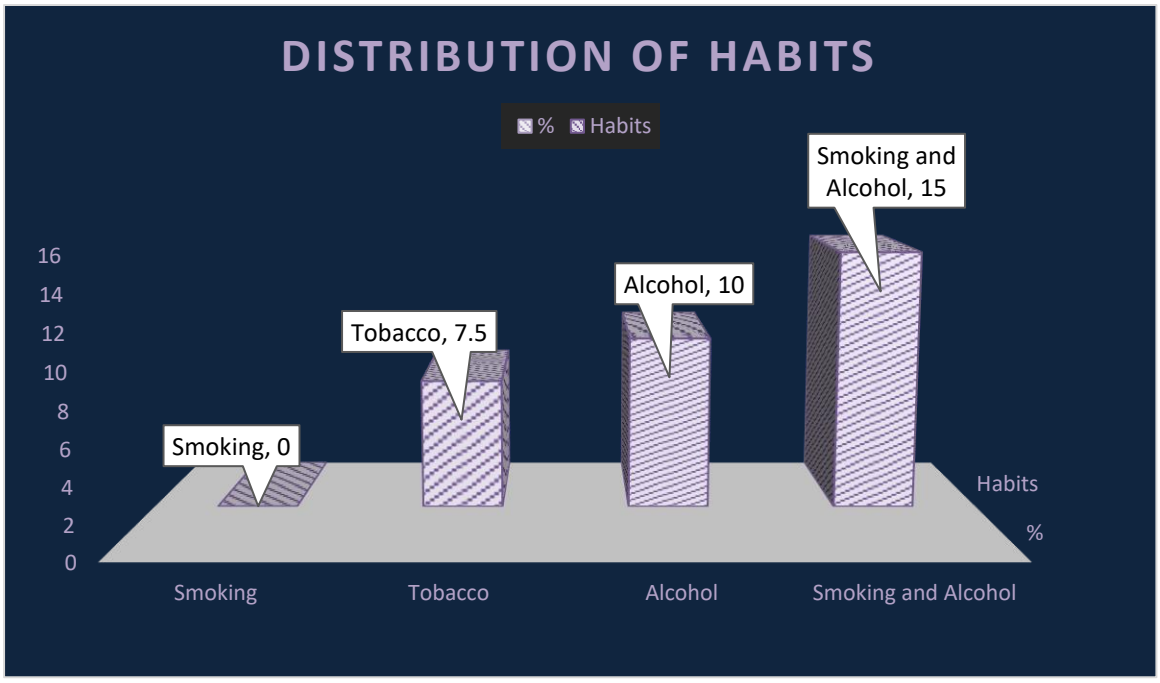


Figure.5.7.8.Distribution of habits

Observation:

Out of 40 patients, 67.5 % of patients had no habits 0% of patients had smoking habits, 7.5% of patients had tobacco chewing habits, Smoking and alcohol 15 % and 10% of patients had alcohol consuming habits.

5.7.9.Thinai Reference:

Sl. No	Thinai	No. of Cases	Percentage
1	Kurinji (Hill Area)	7	17.5%
2	Mullai (Forest Area)	8	20%
3	Marutham (Fertile Land)	3	7.5 %
4	Neithal (Coastal Area)	22	55 %
5	Paalai (Desert Land)	0	0%

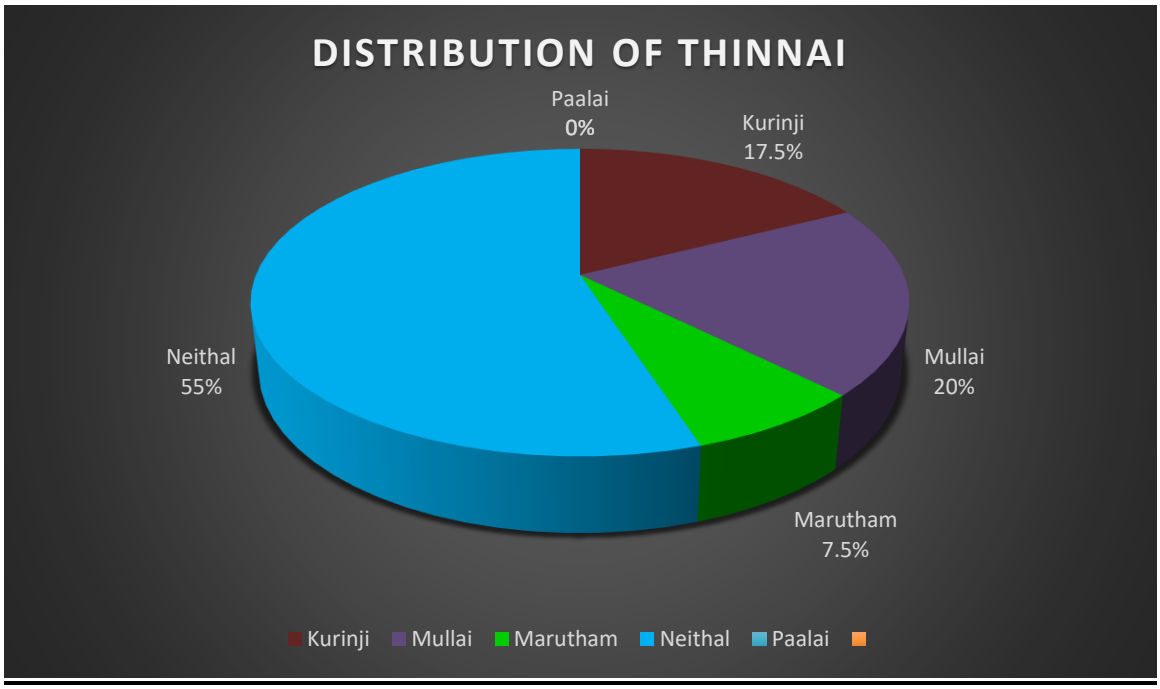


Figure 5.7.9 Thinai Reference

Observation:

7.5% of the patients were from Marutham (Fertile Land) , 17.5% of the patients were fromKurinji (Hill Area),20% of the patients were fromMullai (Forest Area) and the remaining 55% from Neithal (Coastal Area).

5.7.10.Incidence of Kalanjagapadaiin various Paruvakaalam:

Sl. No.	ParuvaKaalam	No. of Cases	Percentage
1	Kaar kaalam (Aavani & Purattasi)	15	37.5 %
2	Koothir Kaalam (Aippasi&Kaarthigai)	7	17.5 %
3	Munpani Kaalam (Margazhi& Thai)	18	45 %

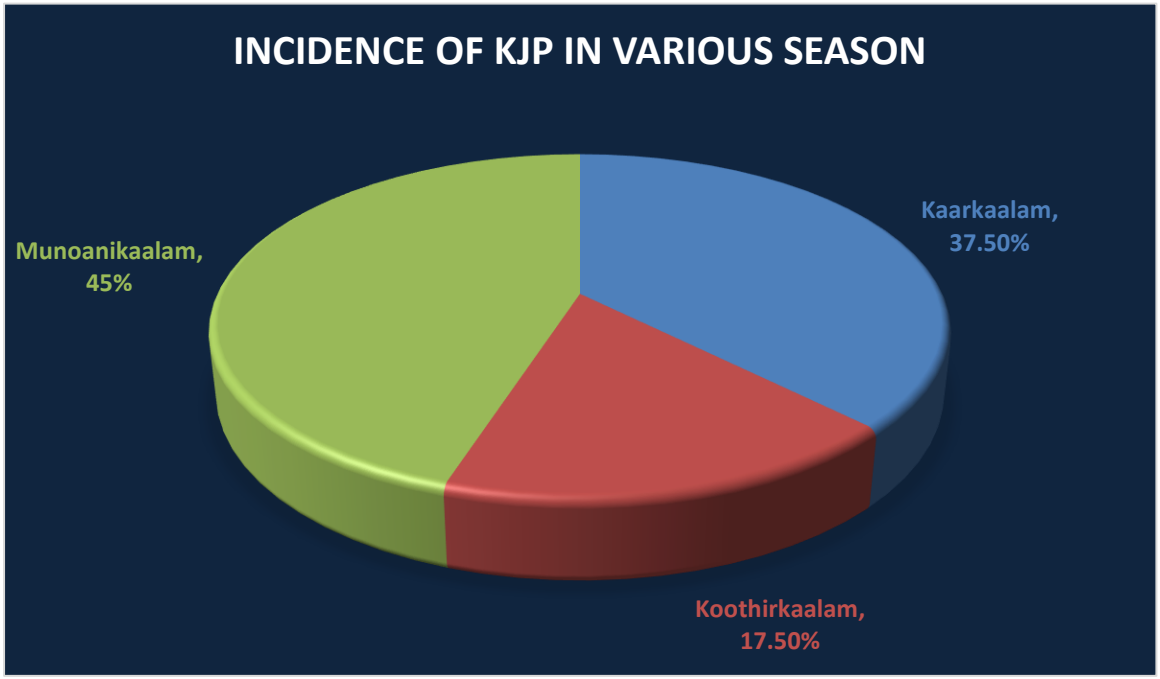


Figure 5.7.10 Incidence of Kalanjagapadai in various Paruvakaalam

Observation:

Patient enrollement period was various seasons especially Kaar kaalam,Koothir kaalam, Munpanikaalam only and didn't enroll of patient in other seasons.

In this study, the highest number of patients reported in Munpani kaalam.

5.7.11.Body constitution of the trial participants (YaakaiIlakkanam):

Sl. No	YaakaiIlakkanam	No. of Cases	Percentage
1	VaathaUdal	13	32.5%
2	PithaUdal	15	37.5 %
3	KabaUdal	3	7.5 %
4	ThonthaUdal	9	22.5 %

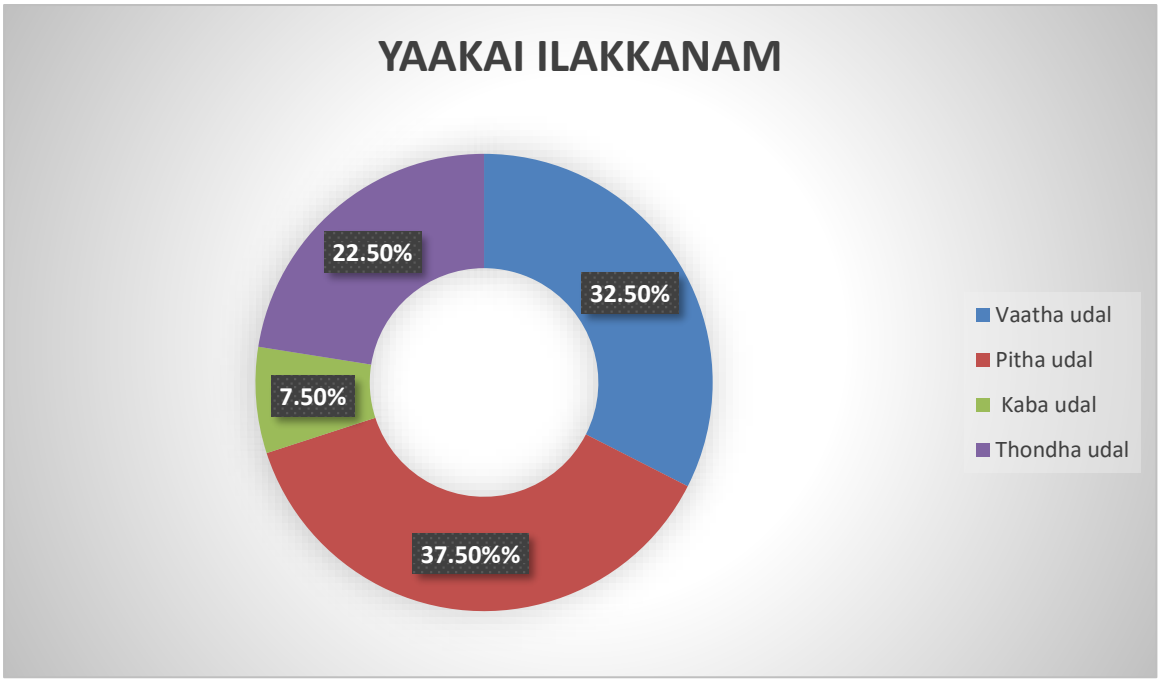


Figure.5.7.11.Yaakai ilakkanam

Observation:

The maximum numbers of patients had Pitha udal (37.5 %)

5.7.12.Distribution of Gunam (Quality and Characters):

Sl. No	Gunam	No of Cases	Percentage
1	Sathuva Gunam	0	0 %
2	Rajo Gunam	40	100 %
3	Thamo Gunam	0	0%

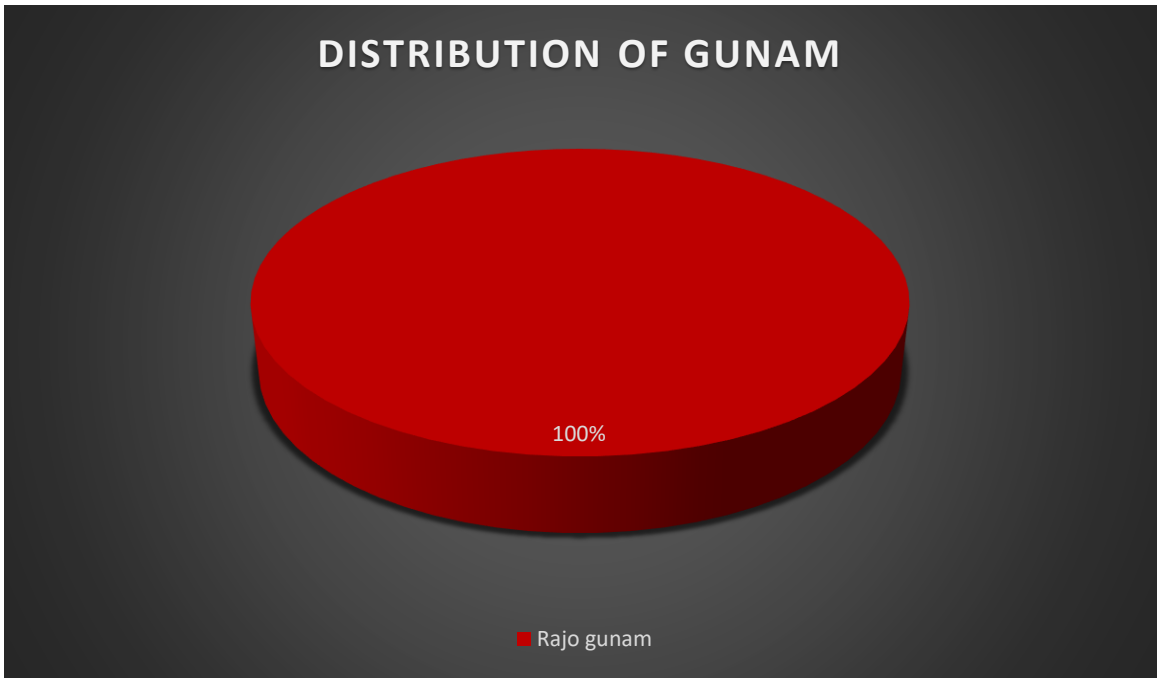


Figure. 5.7.12. Distribution of Gunam

Observation:

100 % of the patients had Rajo Gunam.

5.7.13. Duration of Illness:

Sl. No	Duration of Illness	No of Cases	Percentage
1.	1-6 Months	6	15 %
2.	7-12 Months	0	0 %
3.	1-3 years	14	35 %
4.	4-6 years	12	30 %
s5.	> 6 years	8	20 %

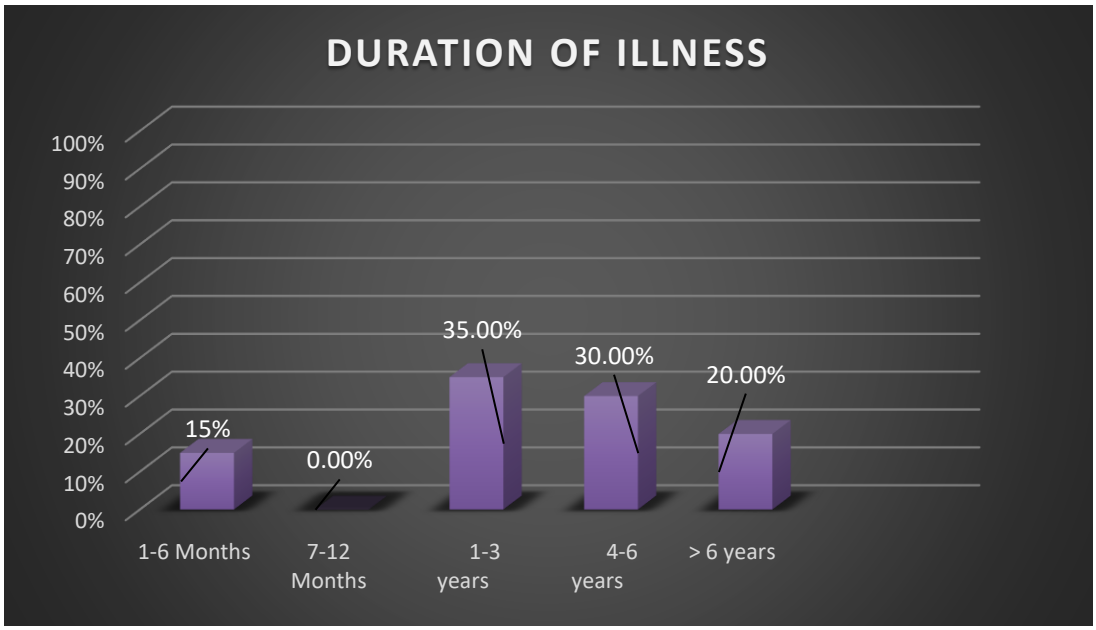


Figure 5.7.13 Duration of Illness

Observation:

35 % of the patients were suffering with during of the illness for 1-3years.

5.7.14.Distribution of Poripulan :

Sl. No	Classification of Poripulan	Before Treatment		After Treatment	
		No of Cases	Percentage	No of Cases	Percentage
1	Mei	40	100 %	11	27.5%
2	Vaai	0	0%	0	0%
3	Kan	0	0%	0	0%
4	Mooku	0	0%	0	0%
5	Sevi	0	0%	0	0%

Observation:

Before treatment mei were found to be affected in all the 40 patients.. After treatment mei were found to be affected in 27.5% of patients.

5.7.15.Distribution of Kanmendhiriyam :

Sl. No	Classification of Kanmendhiriyam	Before Treatment		After Treatment	
		No of Cases	Percentage	No of Cases	Percentage
1	Kai	0	0%	0	0%
2	Kaal	0	0%	0	0%
3	Vaai	0	0%	0	0%
4	Eruvai	01	2.5 %	0	0%
5	Karuvai	0	0%	0	0%

Observation:

Before treatment eruvai were found to be affected in one patients.. After treatment eruvai were found to be no abnormalities.

5.7.16.Distribution of Kosam :

Sl. No	Classification of Kosam	Before Treatment		After Treatment	
		No of Cases	Percentage	No of Cases	Percentage
1	Annamayakosam	03	7.5 %	0	0%
2	Pranamayakosam	01	2.5 %	01	2.5 %
3	Manomayakosam	40	100 %	13	32.5 %
4	Vingnanamayakosam	0	0%	0	0%
5	Anandhamayakosam	0	0%	0	0%

Observation:

Before treatment were found to be affected 7.5% patients in annamayakosam, 2.5% in pranamayakosam,100% in manomayakosam. After treatment were found to be affected 0% patients in annamayakosam, 2.5% in pranamayakosam,32.5% in manomayakosam.

5.7.17.Distribution of Mukkutram

The derangement of Vaatham, Pitham and Kabam in Kalanjagapadai are as follows.

Vaatham

Sl. No	Classification of Vaatham	Before Treatment		After Treatment	
		No of Cases	Percentage	No ofCases	Percentage
1	Pranan	01	2.5 %	1	2.5 %
2	Abanan	1	2.5 %	0	0%
3	Udhanan	40	100 %	16	40 %
4	Samanan	40	100 %	16	40 %
5	Viyanan	40	100 %	16	40 %
6	Nagan	0	0%	0	0%
7	Koorman	0	0%	0	0%
8	Kirukaran	03	7.5%	0	0%
9	Devathathan	9	22.5 %	0	0%
10	Dananjayan	0	0%	0	0%

Observation:

Before treatment Udhanan,Samanan and Viyanan were found to be affected in all the 100% patients.Pranan was found to be in 2.5% of patients, Abanan was found to be in 2.5% of patients, Kirukaran was found to be in 7.5% of patients, Devathathan was found to be affected in 22.5% of patients. After treatment Udhanan,Samanan and Viyanan were found to be affected in 40% of patients. Pranan was found to be in 2.5% of patients.

Pitham

Sl. No	Classification of Pitham	Before Treatment		After Treatment	
		No of Cases	Percentage	No of Cases	Percentage
1	Anarpitham	03	7.5%	0	0%
2	Ranjagapitham	40	100 %	11	27.5 %
3	Sathagapitham	0	0%	0	0%
4	Pirasagapitham	40	100 %	11	27.5 %
5	Alosagapitham	0	0%	0	0%

Observation:

Before treatment Ranjagapitham,Prasagapitham was affected in all the cases and anarpitham was affected in 7.5% patients. After treatment Ranjagapitham,Prasagapitham was affected in 27.5% patients.

Kabam :

Sl. No	Classification of Kabam	Before Treatment		After Treatment	
		No of Cases	Percentage	No of Cases	Percentage
1	Avalambagam	01	2.5 %	01	2.5 %
2	Kiledhagam	03	7.5%	0	0%
3	Pothagam	0	0%	0	0%
4	Tharpagam	0	0%	0	0%
5	Sandhigam	0	0%	0	0%

Observation:

Before treatment kiledhagam was affected in 7.5%.Before and after treatment Avalambagam thee was affected in one case.

5.7.18. Effect of PPK UdalKattukkal:

Sl. No	Udar Kattukkl	Before Treatment		After Treatment	
		No of Cases	Percentage	No of Cases	Percentage
1	Saaram	40	100%	11	27.5%
2	Senneer	40	100%	11	27.5 %
3	Oon	40	100%	11	27.5 %
4	Kozhuppu	0	0%	0	0%
5	Enbu	0	0%	0	0%
6	Moolai	0	0%	0	0%
7	Sukkilam/Suronitham	0	0%	0	0%

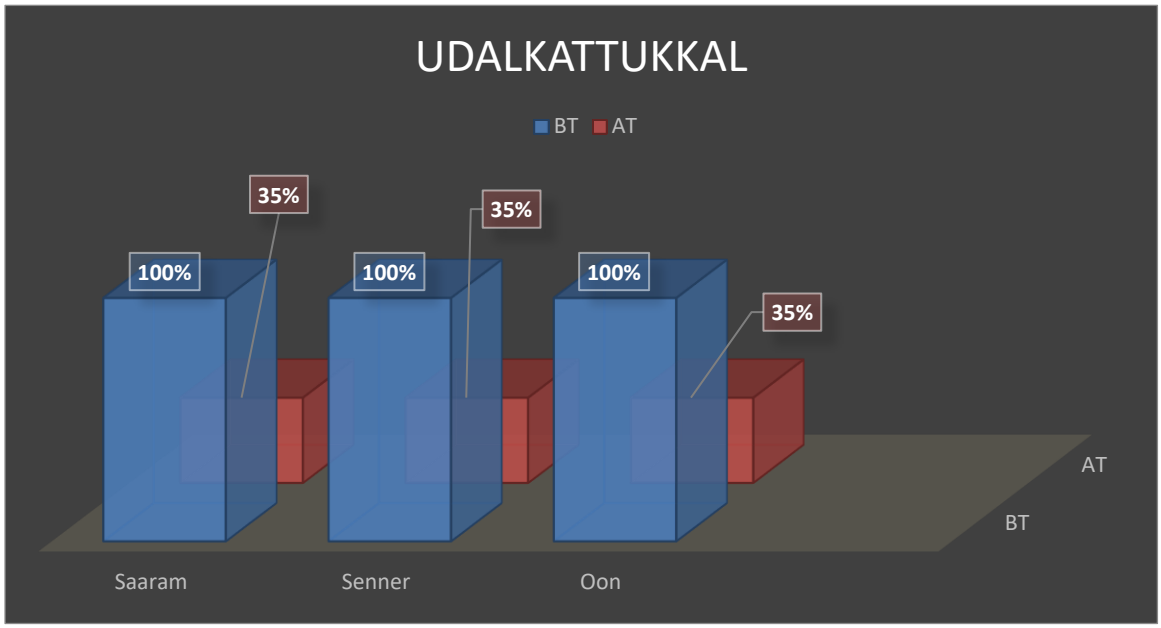


Figure 5.7.14. Effect of PPK UdalKattukkal

Observation:

Before treatment ; Saaram and Seneer, Oon were affected in 100% of cases. After treatments Saaram, Seneer, Oon were affected in 27.5% of cases.

5.7.19. Effect of PPK on Envagai Thervugal:

Sl. No	Envagai Thervugal	Before Treatment		After Treatment	
		No. of Cases	Percentage	No. of Cases	Percentage
1	Naadi				
	a. Vaathapitham	2	5 %	31	77.5 %
	b. Pithavaatham	25	62.5	8	20 %
	c. Pithakabam	7	17.5 %	1	2.5 %
	d. Kabapitham	1	2.5 %	0	0%
	e.Vathakabam	5	12.5 %	0	0%
2	Sparisam	40	100 %	11	27.5 %
3	Naa	0	0%	0	0%
4	Niram	40	100 %	11	27.5 %
5	Mozhi	0	0%	0	0%
6	Vizhi	0	0%	0	0%
7	Malam	1	2.5 %	0	0%
8	Moothiram	0	0%	0	0%

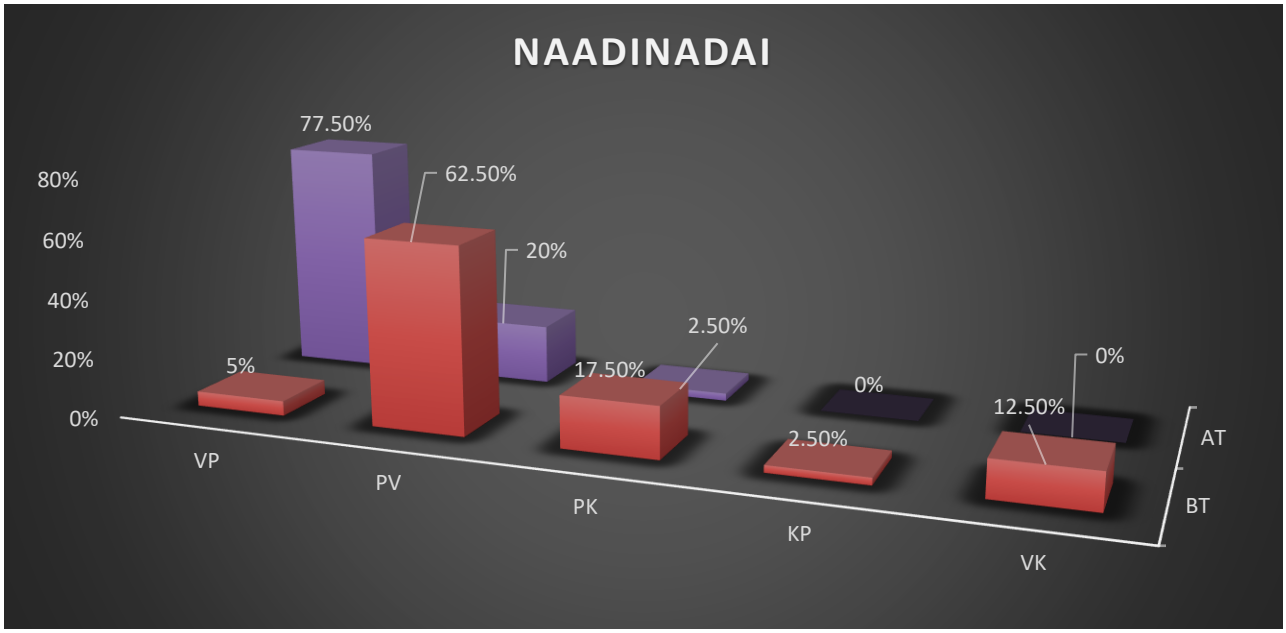


Figure. 5.7.15.Nadinadai in PPK treated patients before and after treatment

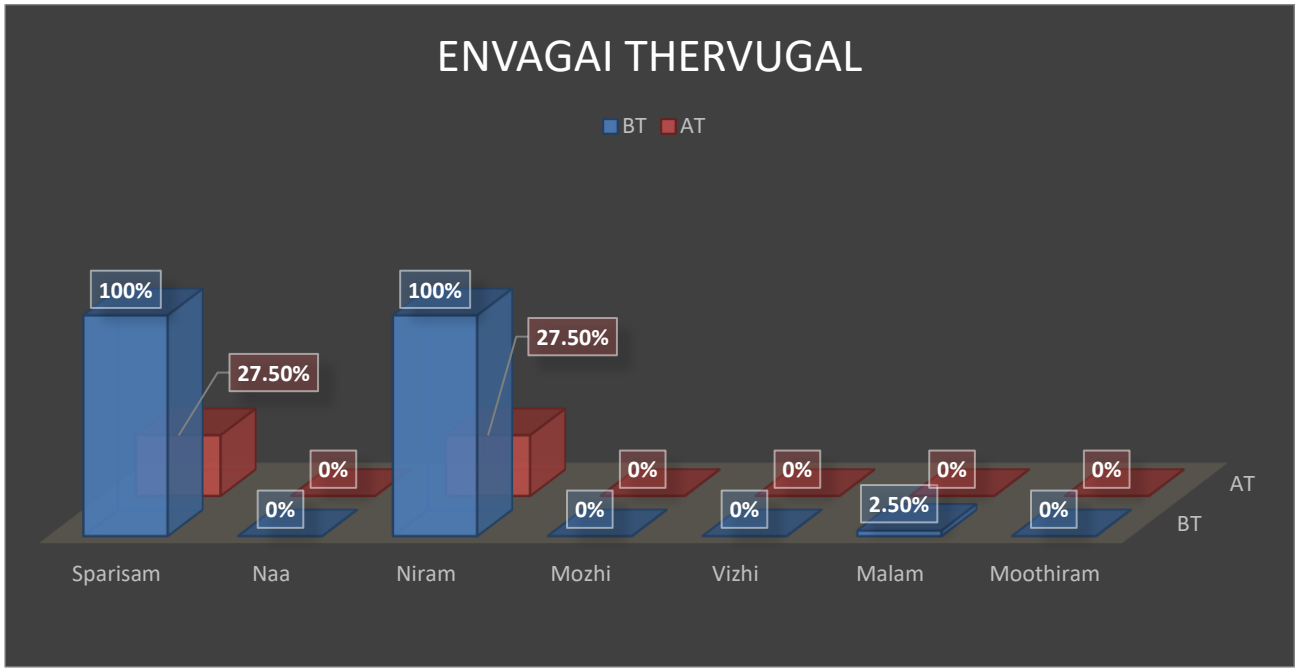


Figure 5.7.16. Effect of PPK on Envagai Thervugal

Observation:

In Envagai thervugal, before treatment Niram and Sparisam were found affected in all the 40 cases, Malam was found affected in 1 cases. The Naadinadai seen in Kalanjagapadai patients were Vaathapitham 5%, Pithavaatham 62.5 %, Pithakabam 17.5 %, Kabapitham 2.5%, Vathakabam 12.5%. After treatment Niram,sparisam affected in 11 cases, The Naadi nadai seen in Kalanjagapadai patients were Vaathapitham 77.5%, Pithavaatham 20 %, Pitha kabam 2.5 %.

Neerkkuri, Neikkuri Inference:

Sl. No	Type of Test	BT No. of Cases	Percentage	AT No. of Cases	Percentage
I	**Neerkkuri: Niram - Colour :**				
1	Hey soaked rain water colour	5	12.5 %	22	55 %
2	Wild *Citrus medica* fruit colour	15	37.5%	2	5 %
3	*Citrus aurantium* fruit colour	19	47.5%	16	40 %
4	Reddish yellow colour	1	2.5 %	0	0 %

II	**Neikkuri pattern**	**1st day**	**Percentage**	**15th day**	**Percentage**	**49th day**	**Percentage**
1	Vatham (Serpentine, Irregular)	0	0 %	0	0 %	02	5%
2	Pitham (Ring)	0	0 %	5	12.5 %	12	30 %
3	Kabam (Pearl)	22	55 %	15	37.5 %	5	12.5 %
	Mixed:	**1st day**	**Percentage**	**15th day**	**Percentage**	**49th day**	**Percentage**
4	VP	02	5 %	5	12.5 %	1	2.5 %
5	PP	2	5 %	0	0%	0	0%
6	PV	01	2.5 %	2	5 %	10	25 %
7	PK	0	0 %	0	0 %	4	10 %
8.	VK	0	0%	1	2.5%	0	0%
8	Mukkuttram	1	2.5 %	1	2.5 %	1	2.5 %
9	Saladaikan (Seive filter holes pattern)	12	30 %	11	27.5 %	5	12.5 %

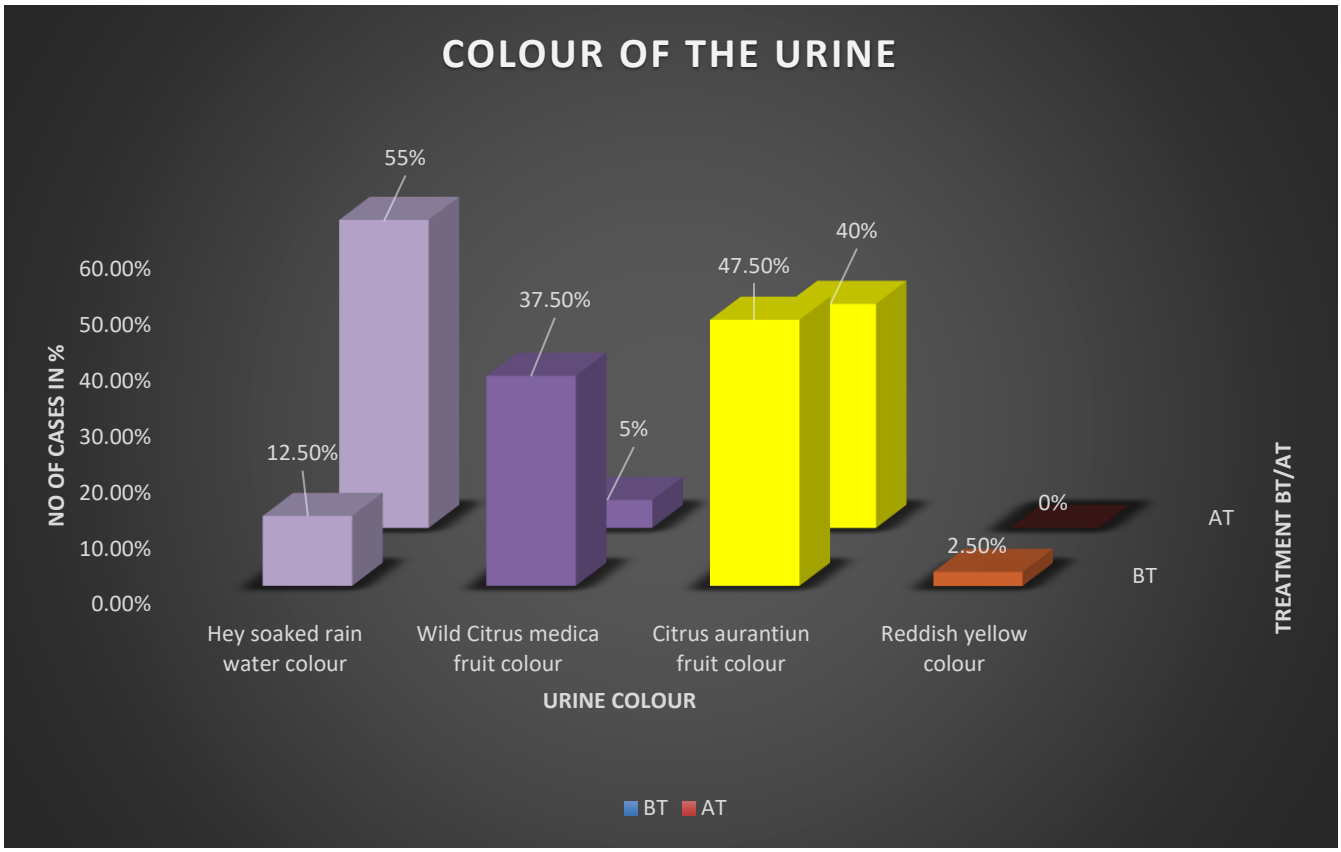


Figure. 5.7.17. Neerkkuri Reference

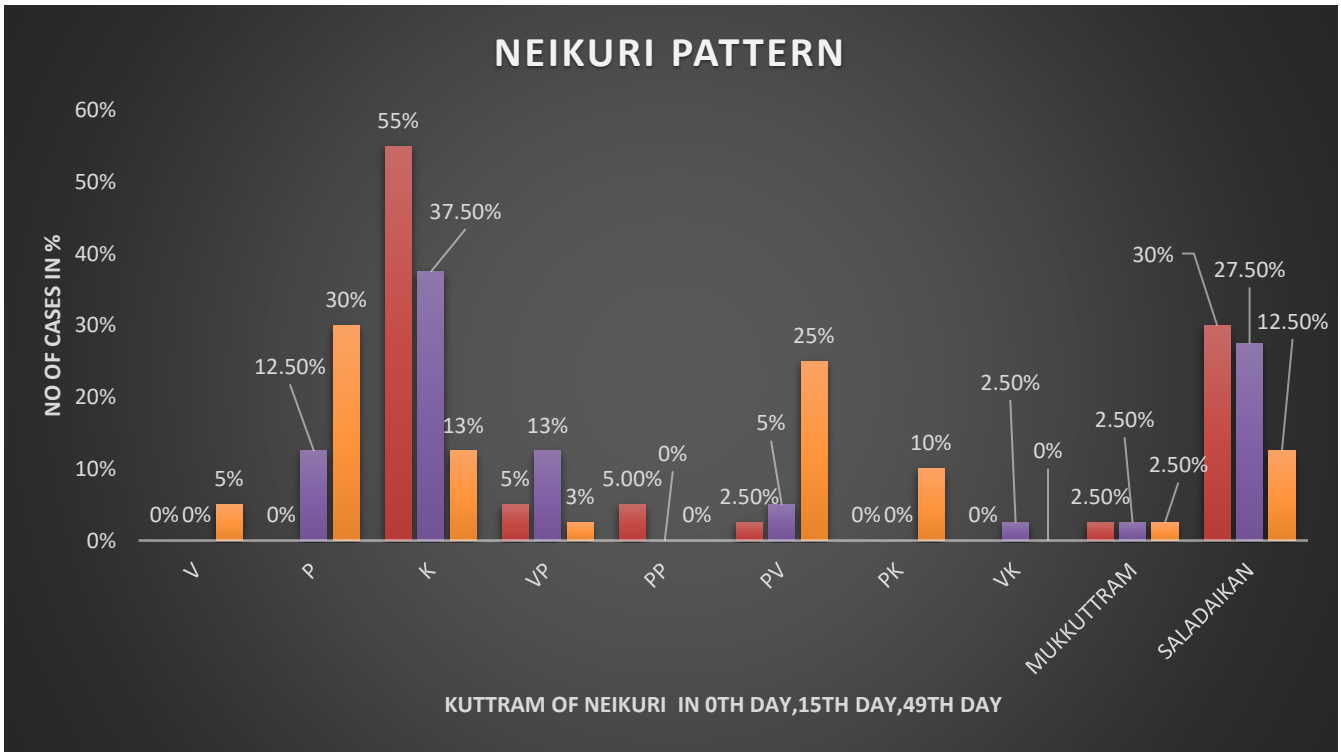


Figure. 5.7.18. Neikkuri Reference

Observation:

In this study ;

On Neerkuri ; before treatment the majority of patients had *Citrus aurantium* fruit colour (47.5%) and wild *citrus medica* fruit colour 37.5%, Hey soaked rain water colour 12.5%,Reddish yellow colour 2.5%.After treatmentthe majority of patients had *Citrus aurantium* fruit colour (40%) and wild *citrus medica* fruit colour 5%, Hey soaked rain water colour 55%.

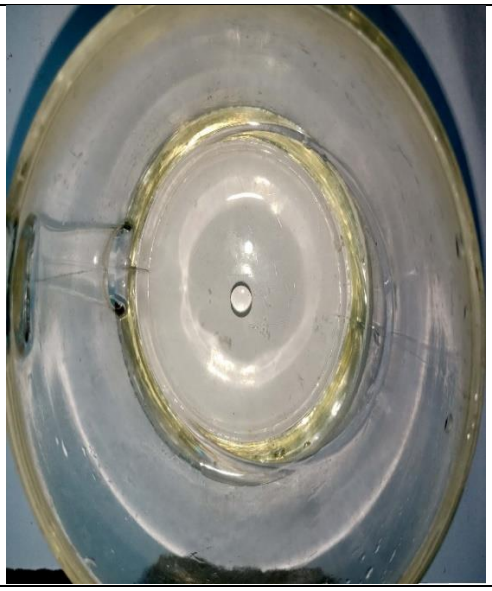
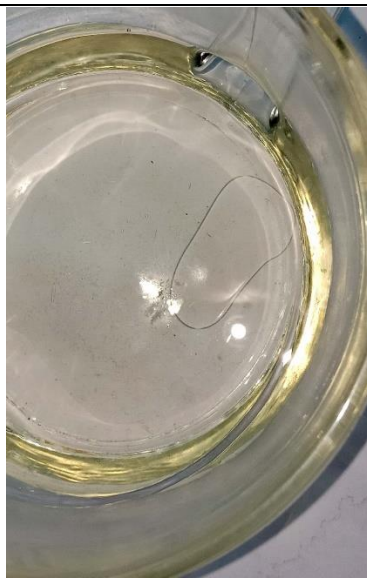
On Neikuri :

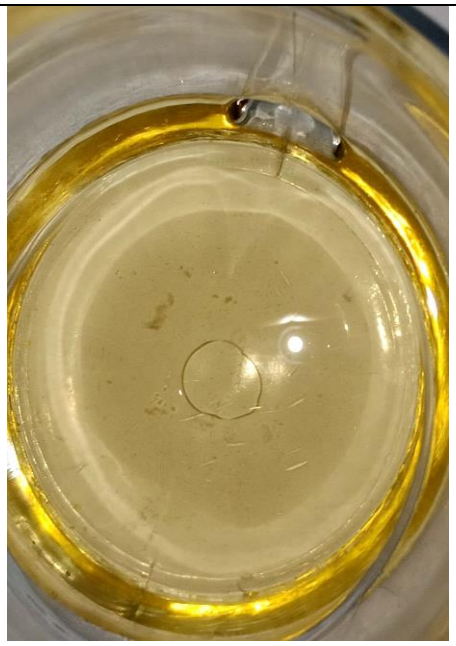
On 1st day the patients had Kabam (Pearl) Neikuri pattern (55%), VP Neikuri pattern (5%),PP Neikuri pattern (5%), PV Neikuri pattern (2.5%), Mukkuttram Neikuri pattern(2.5%) and Severe Kabam (Saladaikan pattern) (30%).

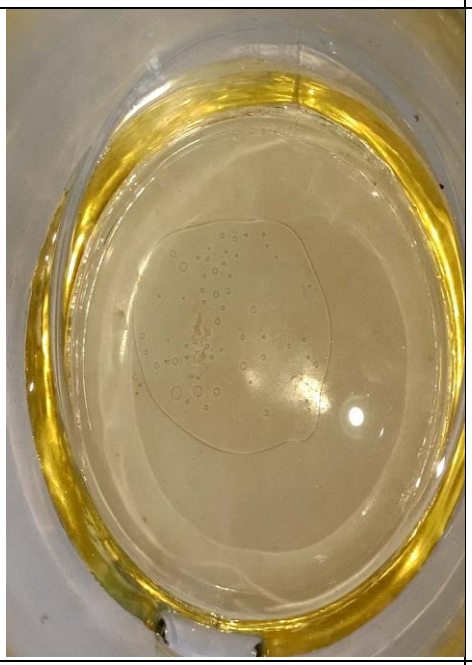
On 15^{th} day the patients had Kabam (Pearl) Neikuri pattern (37.5%),Pitham Neikuri pattern(12.5%) , VP Neikuri pattern (12.5%), PV Neikuri pattern (5%),VK Neikuri pattern (2.5%),Mukkuttram Neikuri pattern (2.5%) and Severe Kabam (Saladaikan pattern) (27.5%).

On 49^{th} day the patients had Vatham Neikuri pattern (5%), Pitham Neikuri pattern (30%),Kabam (Pearl) Neikuri pattern (12.5%), VP Neikuri pattern (2.5%),PV Neikuri pattern (25%),PK Neikuri pattern (10%),Mukkuttram Neikuri pattern(2.5%) and Severe Kabam (Saladaikan pattern) (12.5%).

Figure. 5.7.19.PROGNOSIS OF TREATMENT IN NEIKURI WITHIN 20 MINUTES :

Op no/Age	1st Day:Pasi Score: 72	15th Day Pasi Score : 64.4	49th Day : Pasi Score : 5
F56068/ 60F			
Neikkuri Inference:	*Pearl pattern – Kabam kuttram*	*Irregular with coin pattern - Vatha pitham*	*Aazhi pattern – Pitham kuttram*
Op no/Age	1st Day:Pasi Score: 32.4	15th Day Pasi Score : 28	49th Day : Pasi Score : 2.4
K26618/ 32M			
Neikkuri Inference:	*Pearl pattern –Kabam kuttram*	*Irregular with coin pattern - Vatha pitham*	*Irregular pattern – Vatham kuttram*

Op no/Age	1st Day:Pasi Score: 21	15th Day Pasi Score : 13.5	49th day Pasi Score: 3.3
K98126/ 48M			
Neikkuri Inference:	*Azhiyil azhi pattern* – ***Severe pitham kuttram***	*Aazhi pattern* – ***Pitha kuttram***	*Kalasam pattern* – ***Pithavatham kuttram***
Op no/Age	1st Day:Pasi Score: 28	15th Day Pasi Score : 53.9	49th Day : Pasi Score : 3.3
1526-18/21M			
Neikkuri Inference:	*Pearl pattern* –***Kabam kuttram***	*Irregular with coin pattern* – ***Vatha Pitham kuttram***	*Bottle guard pattern* – ***Pithavatham kuttram***

Op no/Age	1st Day:Pasi Score: 35.1	15th Day Pasi Score : 63.6	49th day Pasi Score: 0.3
1709-19/50M			
Neikkuri Inference :	*Saladaikan (Seive filter holes) pattern – Severe Kabam kuttram*	*Saladaikan (Reduced number and size of Seive filter holes) pattern – Severe Kabam kuttram*	*Aazhi pattern – Pitham kuttram*
Op no/Age	1st Day:Pasi Score: 32.1	15th Day Pasi Score : 26.1	49th Day : Pasi Score : 0.4
0033-19/34M			
Neikkuri Inference :	*Regular with irregular size coin pattern – Pithathil pitham kuttram*	*Irregular with Seive filter hole pattern – Vatham Kabam kuttram*	*Pearl pattern – Kabam kuttram*

Op no/Age	1st Day:Pasi Score: 72	15th Day Pasi Score : 19.7	49th Day : Pasi Score : 0
0221-19/33M			
Neikkuri Inference :	*Irregular with Irregular coin pattern – Vatham Pitham kuttram*	*Irregular with Irregular coin pattern – Vatham Pitham kuttram*	*Irregular pattern – Vatham kuttram*

5.7.20.MANIKADAI NOOL :

Sl. No	Finger breadth	Before Treatment	
		No of Cases	Percentage
1.	7 ¾	1	2.5 %
2.	8	2	5 %
3.	8 ¼	0	0%
4.	8 ½	29	72.5 %
5.	8 ¾	0	0%
6.	9	2	5 %
7.	9 ¼	1	2.5 %
8.	9 ½	1	2.5 %
9.	9 ¾	1	2.5 %
10.	10	1	2.5 %
11.	11	2	5 %

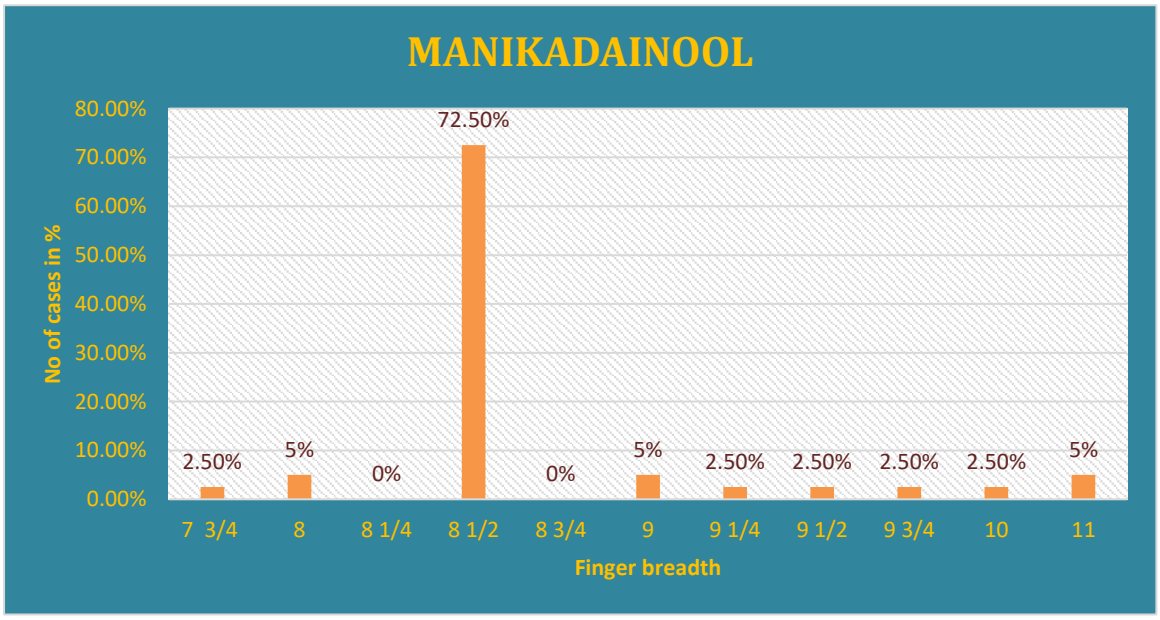


Figure. 5.7.20.Manikadainool

Observation:

In this study, before treatment the majority of patients had 8 ½ finger breadth (72.5%)

5.7.21.MEDICINE STARTING DAY :

Sl. No	DAY	No of Cases	Percentage	Prognosis & no of cases	
1	Sunday	18	45 %	Good	16
				Moderate	2
				Poor	0
2	Tuesday	11	27.5 %	Good	7
				Moderate	3
				Poor	1
3	Thursday	11	27.5 %	Good	5
				Moderate	3
				Poor	3

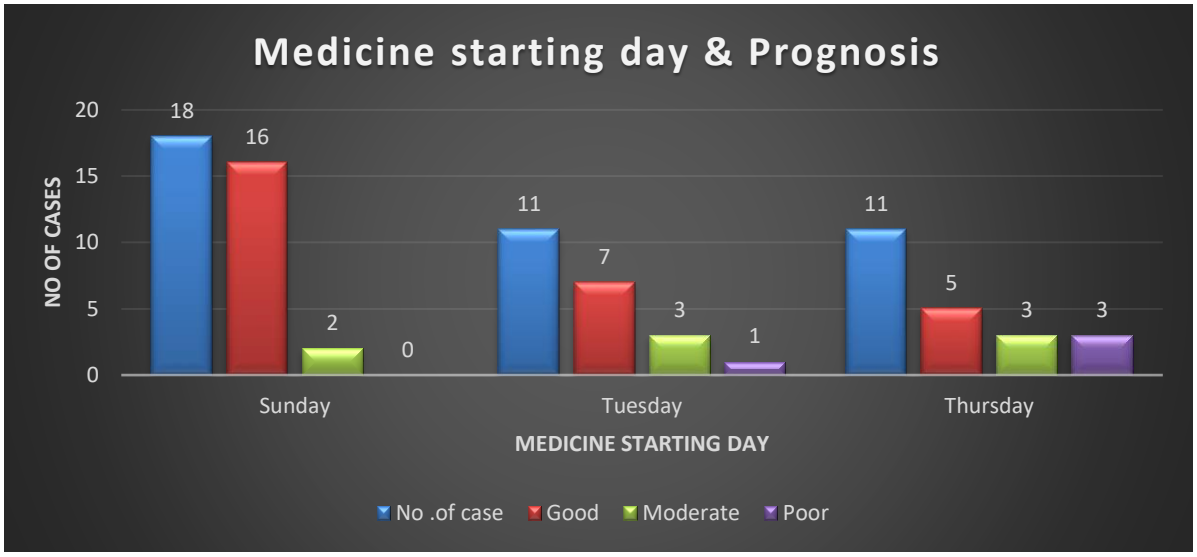


Figure. 5.7.21.Medicine started day and their prognosis

Observation:

In this study, 45% of patients started medicine on Sunday,27.5% of patients started medicine on Tuesday ,27.5% of patients started medicine on Thursday.The majority of patient had medicine on Sunday with good improvement.

5.7.22.Effect of PPK on Haematological parameters:

Treatment	Hb (gm/dl)	WBC (cells/cu.mm)	RBC (million/cu.mm))	PLT (lak/cu.mm)
Before Treatment	13.92 ±1.82	7747.50±2108.10	4.77 ±0.56	2.83 ±0.67
After Treatment	13.92 ± 1.48	7352.50±1505.03	4.80 ±0.55	2.77±0.69
Two tailed p value	0.9999	0.3378	0.8096	0.6942
t value	0.000	0.9645	0.2417	0.3946

Inference:

The Hematological parameters tested for the patients treated with PPK that there was no major difference both before and after treatment. This result proved for the safety of the trial drug adminstered as the values were well within normal limits.Values expressed in Mean ± SEM; Statistical analysis was performed using Student 't' test using Graph Pad Prism 3.1.

5.7.23.Effect of PPK on Biochemical parameters:

Biochemical parameters					
Treatment	**Glucose-FBS (mg/dl)**	**Cholesterol (mg/dl)**	**Triglycerides (mg/dl)**	**SGOT (IU/l)**	**SGPT (IU/l)**
Before Treatment	93.17±12.91	180.03±32.62	126.61±60.20	23.14±8.24	24.61±11.77
After Treatment	87.97±15.43	172.25±34.88	143.27±79.35	26.02±10.98	28.72 ±18.49
Two tailed p value	0.1061	0.3060	0.2934	0.1884	0.2392
t value	1.635	1.030	1.058	1.327	1.186

Biochemical parameters				
Treatment	**ALP (IU/L)**	**Urea (mg/dl)**	**Creatinine (mg/dl)**	**Bilirubin (mg/dl)**
Before Treatment	86.40 ±26.61	18.74±3.72	0.98 ±0.13	0.84±0.46
After Treatment	75.33 ±26.05	18.49±4.66	0.99 ±0.13	0.75±0.37
Two tailed p value	0.0638	0.7916	0.7318	0.3379
t value	1.880	0.2652	0.3440	0.9642

Inference:

The Biochemical parameters tested for the patients treated with PPK that there was no major difference both before and after treatment. This result proved for the safety of the trial drug administered as the values were well within the normal limits. Values expressed in Mean ± SEM ; Statistical analysis was performed using Student 't' test using Graph Pad Prism 3.1

5.7.24.The effect of Parangipaatai Kudineer on the clinical features of the trial Subjects:

Sl. No	**Clinical Features**	**Before Treatment**		**After Treatment**	
		Frequency	**Percentage**	**Frequency**	**Percentage**
1	Erythema	40	100%	17	42.5 %
2	Scaling	40	100%	12	30 %
3	Itching	40	100%	5	1.5 %
4	Fissure	5	12.5 %	0	0%
5	Pustule	3	7.5 %	0	0%
6	Auspitz sign	40	100%	6	15 %
7	Candle Grease sign	40	100%	12	30 %

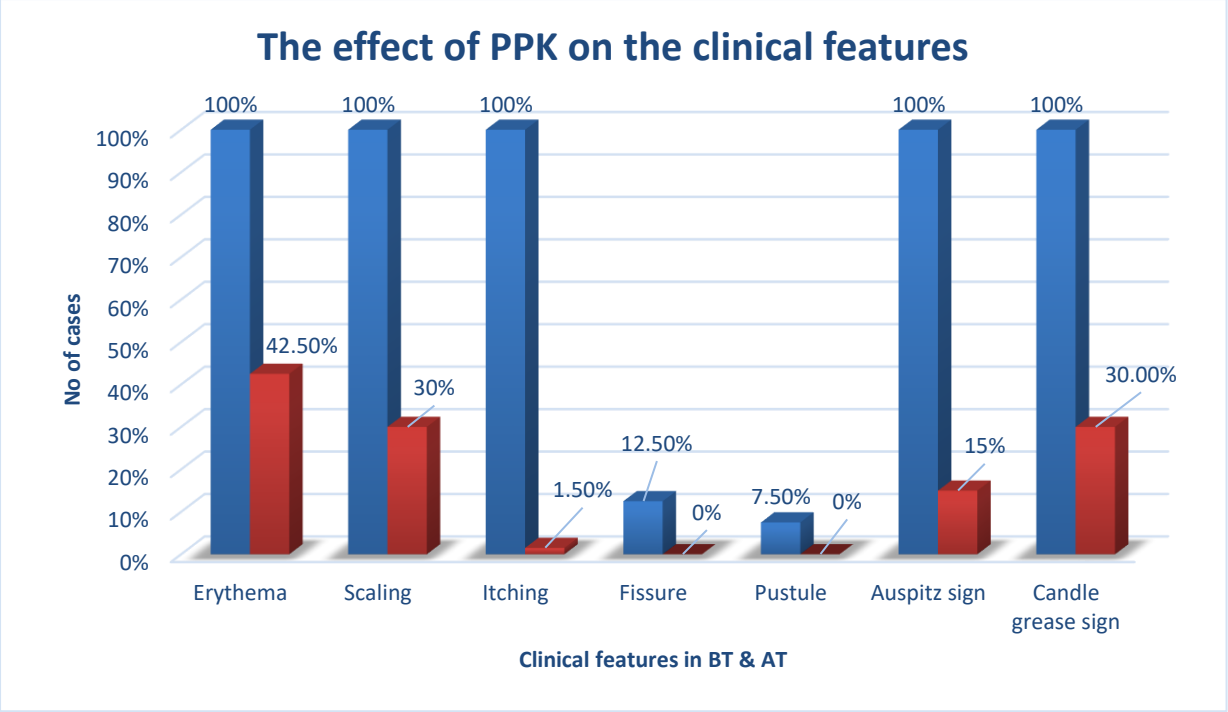


Figure. Figure. 5.7.22. The effect of Parangipaatai Kudineer on the clinical features

Observation:

Before treatment all the patients had the clinical features of erythema, scaling, itching, Auspitz sign, Candle grease sign and 12.5 % of cases had Fissure, 7.5 % of cases had pustule. After treatment 42.5% of cases had erythema, 30% of cases had scaling, 1.5% of cases had itching, 15% of cases had Auspitz sign, 30% of cases had Candle grease sign.

5.7.25.Shape & Site of Lesion

S.NO	**Shape of Lesion**	**No.of Case**	**Percentage**
1	Irregular	37	92.5 %
2	Coin	03	7.5 %
3	Dispersed	0	0%
S.NO	**Site of Lesion**	**No.of Case**	**Percentage**
1	Head	40	100 %
2	Upper limb	40	100 %

3	Lower limb	40	100 %
4	Trunk	40	100 %
5	Nail Changes	02	5 %
6	Palmo plantar	07	17.5 %
7	Joint Involvement	0	0%

Observation:

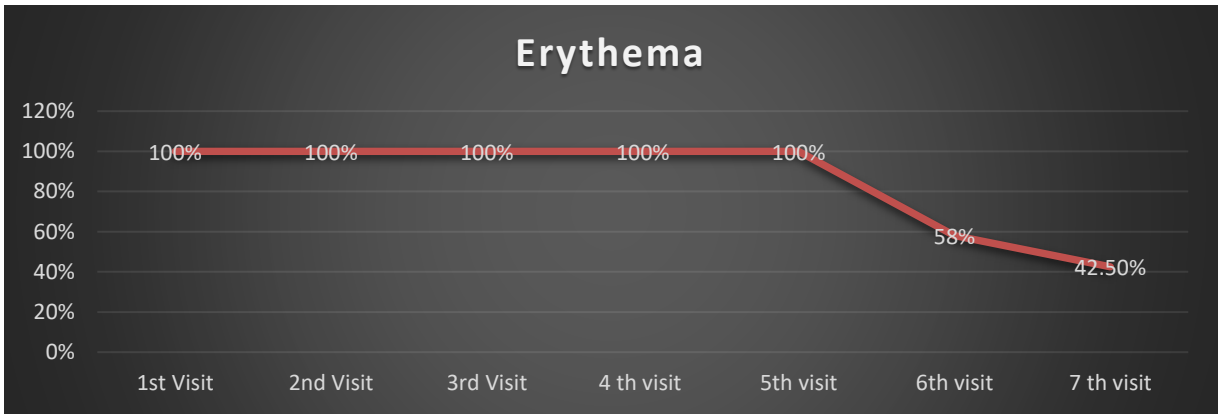
92.5% of cases had irregular shape of lesion.

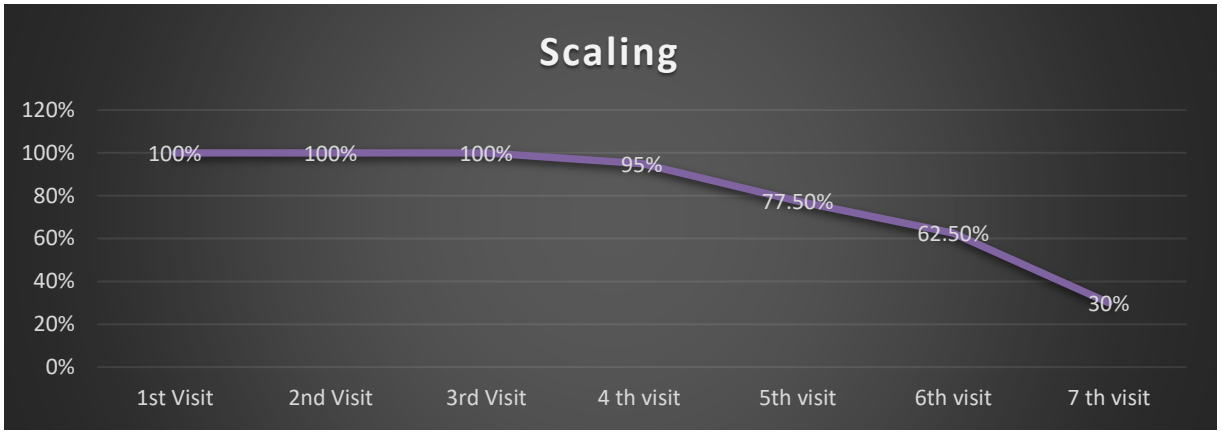
5.7.26.Effect of Parangipaatai Kudineer on Clinical signs/symptoms in each visit:

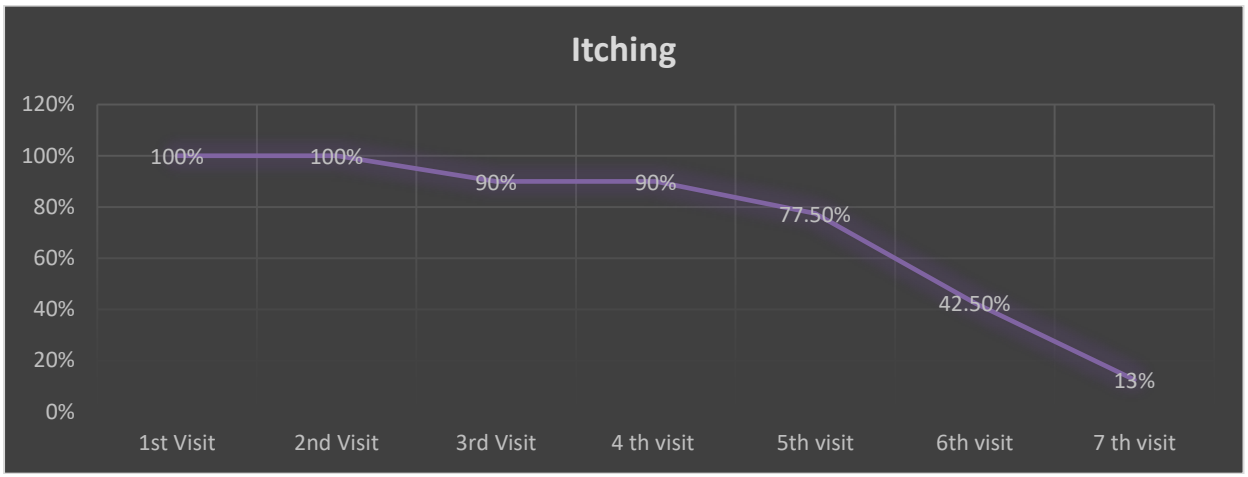
Clinical features	Visit						
	1st	2nd	3rd	4th	5th	6th	7th
Erythema	40	40	40	40	40	23	17
Scaling	40	40	40	38	31	25	12
Itching	40	40	36	36	31	17	5
Fissure	5	4	4	2	1	0	0
Pustule	3	2	0	0	0	0	0
Auspitz sign	40	39	35	26	17	12	6
Candle Grease sign	40	40	39	35	27	15	12

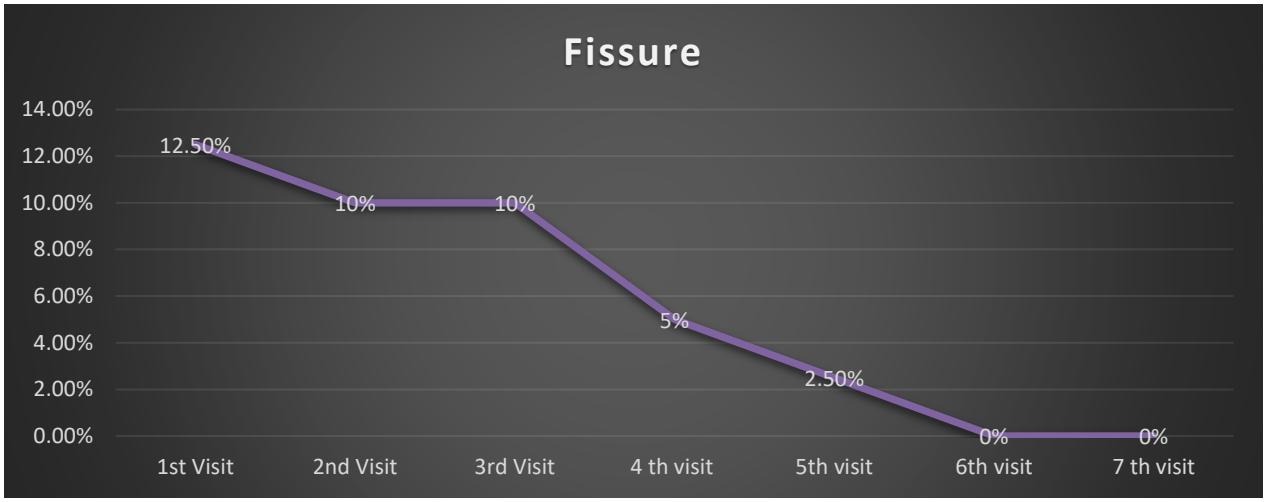
Clinical features	Percentage						
	1st	2nd	3rd	4th	5th	6th	7th
Erythema	100%	100%	100%	100%	100%	57.5 %	42.5 %
Scaling	100%	100%	100%	95 %	77.5 %	62.5 %	30 %
Itching	100%	100%	90 %	90 %	77.5%	42.5 %	12.5 %
Fissure	12.5 %	10 %	10 %	5 %	2.5 %	0 %	0 %
Pustule	7.5 %	5 %	0 %	0 %	0 %	0 %	0 %
Auspitz sign	100%	97.5 %	87.5 %	65 %	42.5 %	30 %	15 %
Candle Grease sign	100%	100%	97.5%	87.5 %	67.5%	37.5%	30 %

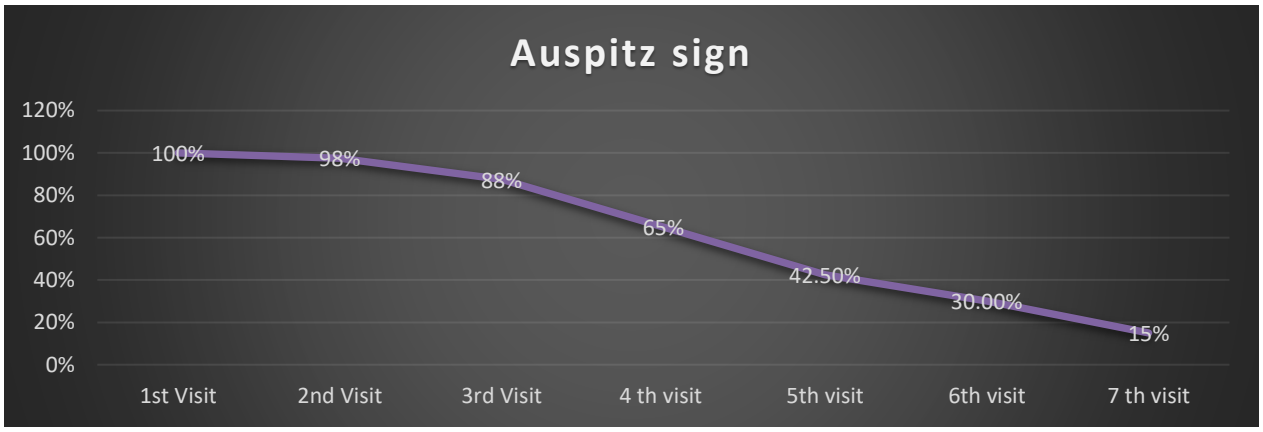
Figure. 5.7..23. Effect of PPK on Clinical signs/symptoms in each visit

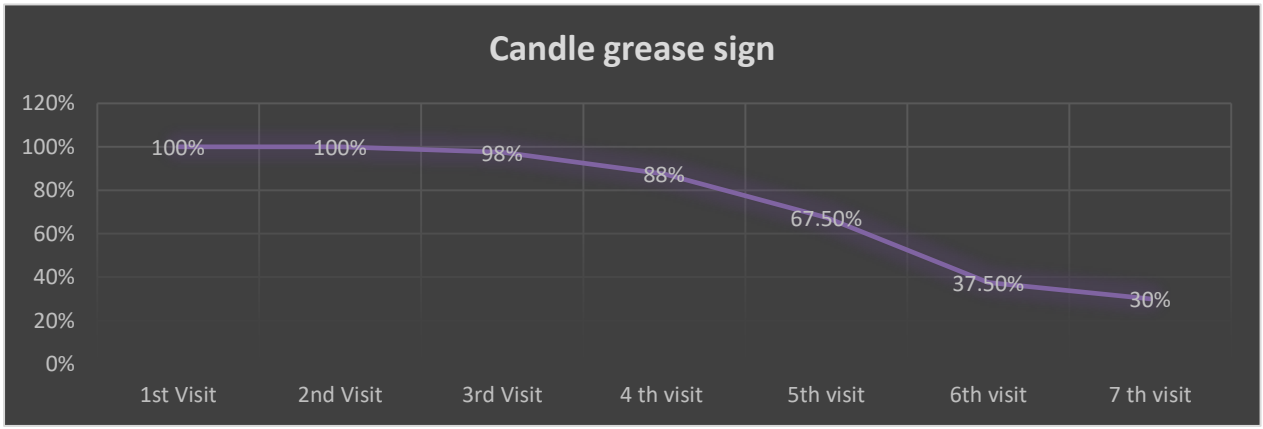












Observation:

The most common discomfort encountered by the patients who had Psoriasis was Itching and scaling. 40 patients out of 40 (100%) had this symptom and the test drug PPK corrected symptom of itching in 87.5% of the patients and corrected symptoms of scaling in 70 % of patients. The symptom of erythema was found all patients (100%). This was cleared in most of the patients (57.5%) who had this complaint.The symptom of fissure (12.5%) ,

pustule (7.5%) was found in the patients. This was cleared all patients who had fissure and pustule complaint.The most common signs in the patients who had Psoriasis was auspitz sign and candle grease sign. 40 patients out of 40 (100%) had this signs and the test drug PPK clear the sign of auspitz sign in 85% of the patients and candle grease sign in 70% of the patients.

5.7.27.Dermatology Life Quality Index score before and after treatment:

S.No	DLQI	Frequency BT	Percentage BT	Frequency AT	Percentage AT
1	Score 0-1	0	**0 %**	19	47.5 %
2	Score 2-5	0	**0 %**	11	27.5 %
3	Score 6-10	0	**0 %**	1	2.5 %
4	Score 11-20	0	**0 %**	7	17.5 %
5	Score 21-30	40	100 %	2	5 %

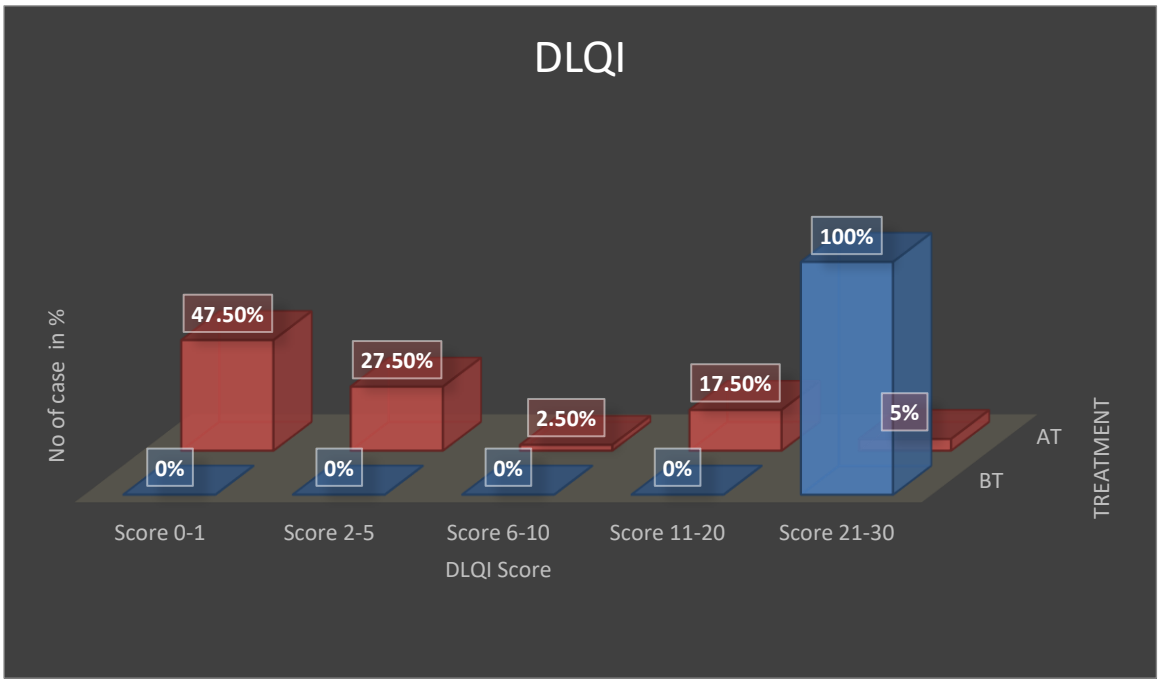


Figure.5.7.24. Dermatology Life Quality Indexscore BT and AT

Observation:

Quality of life score in before treatment score 21-30 in 40 patients. After treatment score 0-1 in 19 patients, score 2-5 in 11 patients, score 6-10 in 1 patients, and score 11-20 in 7 patient. Score 21-30 in 2 patients.

5.7.28.Assessment of Treatment response with PASI Score in Group I : Trail drug without yogam in OPD patients :

Variable	1st Day	8th day	15th day	22nd day	29th day	36th day	43rd day	49th day
MEAN	42.07	43.67	44.43	37.76	31.96	25.06	17.16	12.39
SEM	6.98	7.34	7.11	5.86	5.29	4.45	4.35	5.08

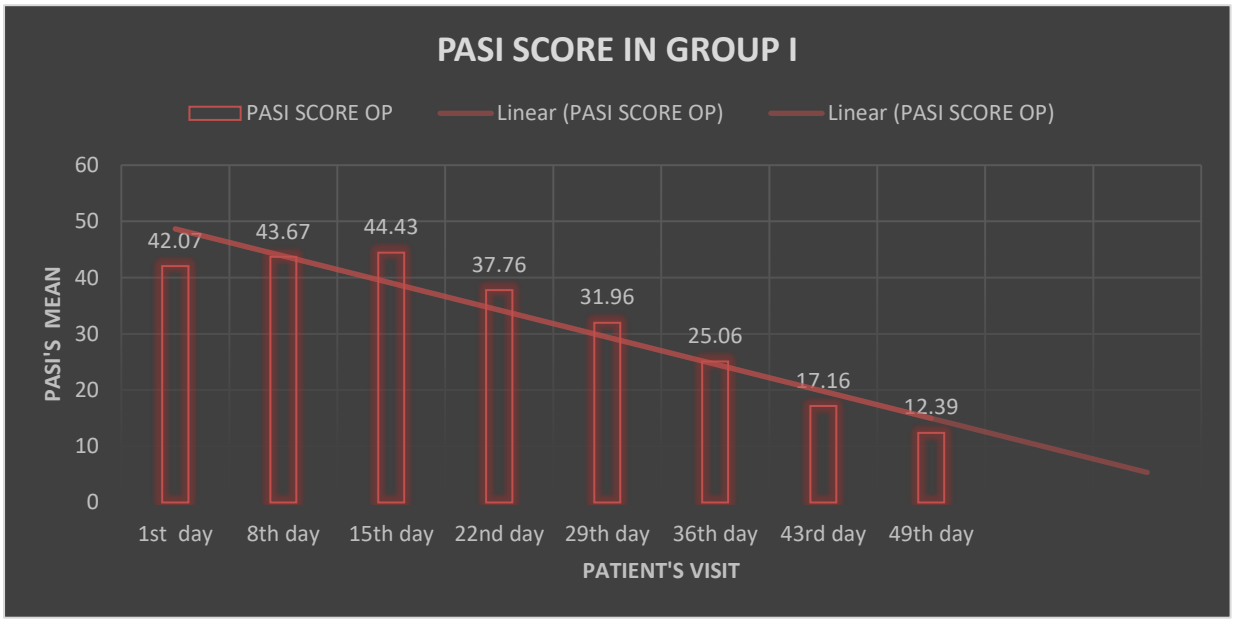


Figure.5.7.25. Treatment response with PASI Score in group I patients

Inference:

Treatment assessment response in group I was shown 42.07±6.98 on first day (BT) and it was 12.39±5.08 on it 49th day (AT).Till 15th day, there is a gradually increase of PASI score i.e. upto 44.43±7.11 and after 15th day of the treatment, the PASI score declines to 12.39±5.08.

Assessment of the Treatment response with PASI Score in Group II : Trail drug with yogam in IPD patients.

Variable	1st Day	8th day	15th day	22nd day	29th day	36th day	43rd day	49th day
MEAN	43.46	43.46	42.90	35.89	26.06	19.18	8.59	4.22
SEM	7.77	7.77	6.72	7.40	6.03	5.82	3.19	2.16

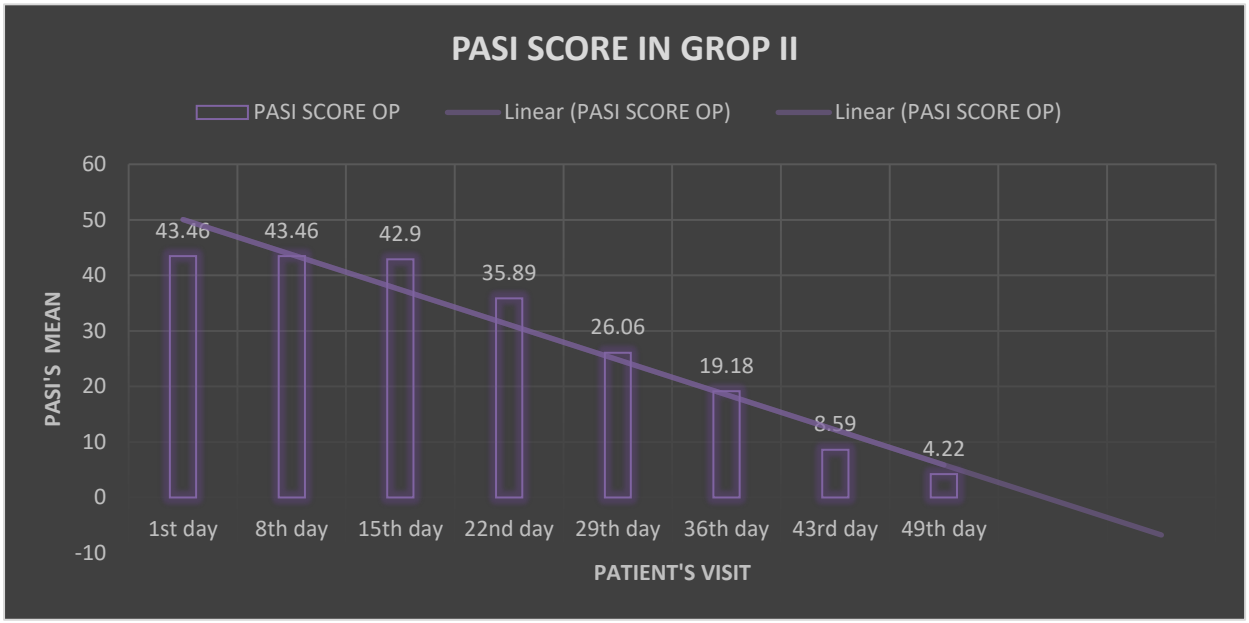


Figure. 5.7.26 Treatment response with PASI Score in group II patients

Inference:

Treatment assessment response in group II was shown 43.46±7.77 on first day (BT) and it was 4.22±2.16 on it 49th day (AT).Till 49th day, there is a gradually declines of PASI score.

Assessment of the Treatment response with PASI Score in both Group patients:

Variable	1st Day	8th day	15th day	22nd day	29th day	36th day	43rd day	49th day
MEAN	42.76	43.56	43.67	36.82	29.01	22.12	12.87	8.3
SEM	7.30	7.46	6.84	6.60	5.75	5.29	4.23	4.27

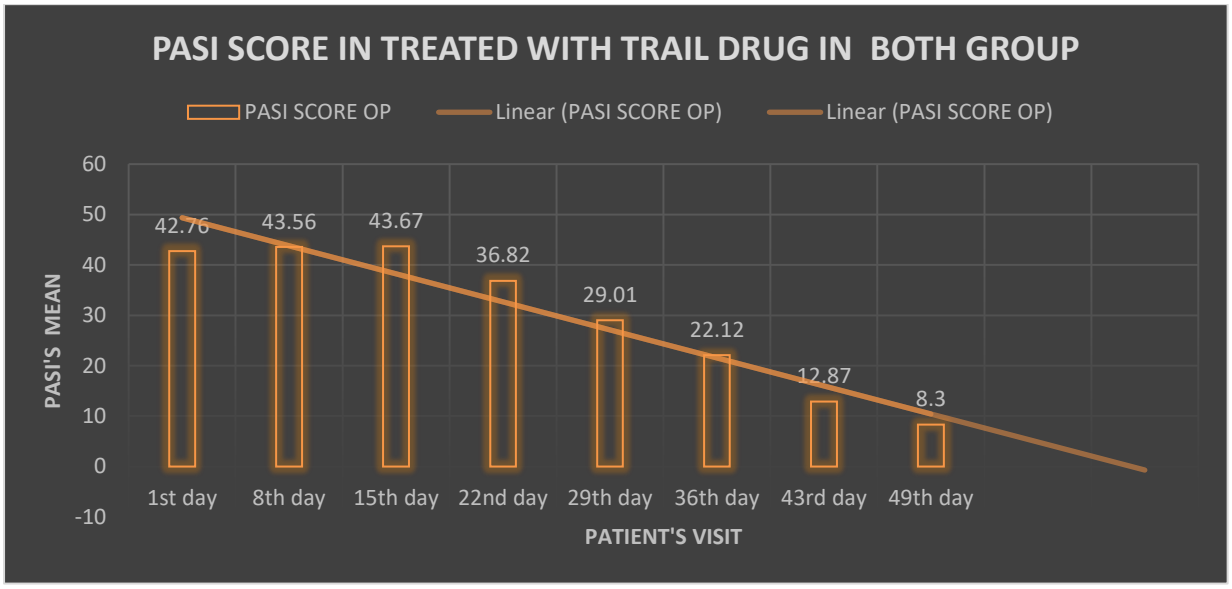


Figure. 5.7.27.Treatment response with PASI Score in both group patients

Inference:

Treatment assessment response in both group (all patient) was shown 42.76±7.30 on first day (BT) and it was 8.3±4.27 on it 49th day (AT).Till 15th day, there is a gradually increase of PASI score i.e. upto 43.67±6.84 and after 15th day of the treatment, the PASI score declines to 8.3±4.27.

Paired Sample Statistics (PASI Score Before Treatment and After Treatment) :

Variable	Sample size	Before treatment	After Treatment	t Value	p Value
Group I Mean±SEM	20	42.07±6.98	12.39±5.08	t = 3.438	p <0.0014
Group II Mean±SEM	20	43.46±7.77	4.22±2.16	t = 4.866	p <0.0001

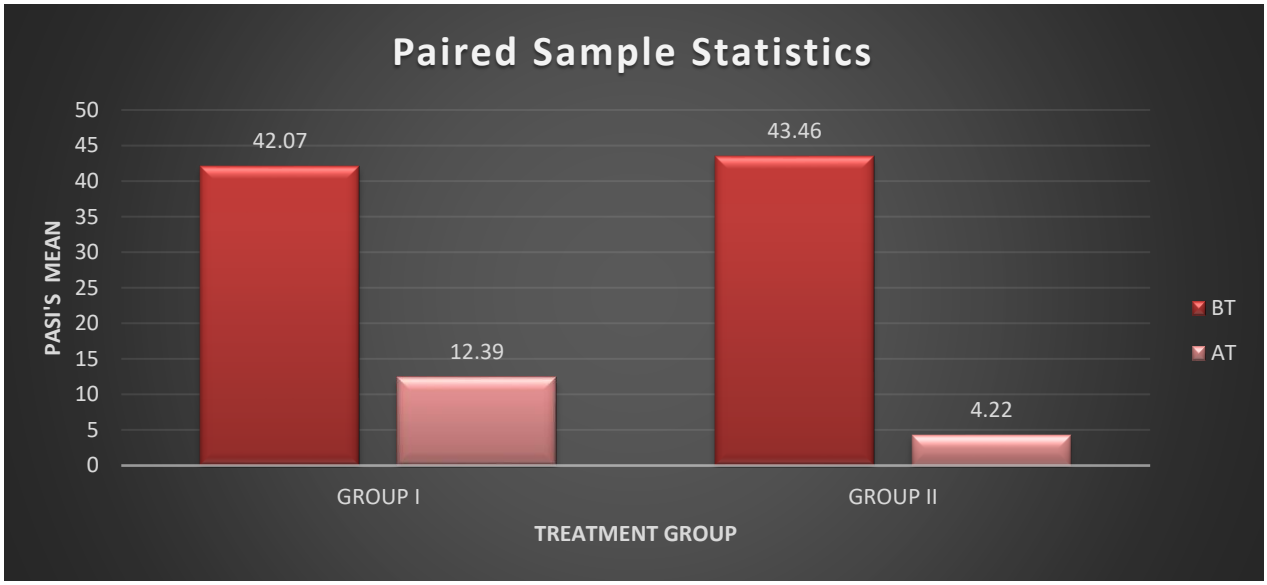


Figure 5.7.28.Paired Sample Statistics

Inference:

The mean± SEM of PASI score at before and after treatment in group I were 42.07±6.98 and 12.39±5.08 respectively which is statistically very significant (t = 3.438, p <0.0014).

The mean± SEM of PASI score at before and after treatment in group II were 43.46±7.77 and 4.22±2.16 respectively which is statistically extremely significant (t = 4.866, <0.0001).

Observation of assessment of treatment response with PASI Score :

According to above the inferences ; Initially the symptoms of psoriasis may be aggravated and then gradually declines by the trail drug.

As per paired sample statistics , Group II (with yogam) was shown excellent outcome of the treatment greaterthan Group I (without yogam).

5.7.29. Outcome:

Sl. No	Results	No of Cases Group I	Percentage	No of Cases Group II	Percentage
1	Good	13	65%	16	80 %
2	Moderate	4	20%	4	20 %
3	Poor	3	15%	0	0 %

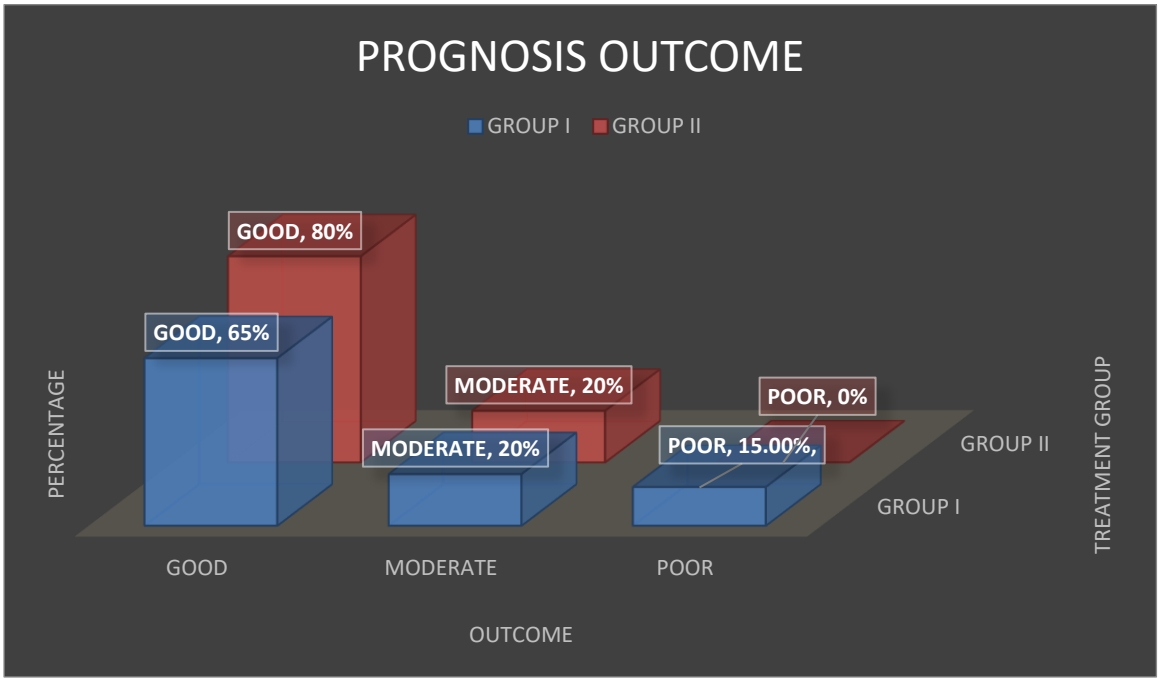


Figure 5.7.29.Outcome

Observation:

The outcome of this study showed promising results. In group I : Good improvement was observed in 13 patients (65%), moderate improvement in 4 patients (20%), and poor improvement in 3 (15%) cases. In group II : Good improvement was observed in 16 patients (80%), moderate improvement in 4 patients (20%).

5.7.30.EFFECT OF THE TRIAL DRUG IN VARIOUS TYPE OF KJP :

Sl. No	TYPE OF PSORIASIS	No of Cases	Percentage	OUTCOME	No of Cases	Percentage
1	Psoriasis vulgaris	27	67.5 %	Good	18	45 %
				Moderate	6	15 %
				Poor	3	7.5 %
2	Psoriasis vulgaris with Pustular psoriasis	1	2.5 %	Good	1	2.5 %
3	Guttate psoriasis	10	25 %	Good	8	20 %
				Moderate	2	5 %
				Poor	0	**0 %**
4	Guttate psoriasis with Pustular psoriasis	1	2.5 %	Good	1	2.5 %
5	Psoriasis vulgaris with inverse psoriasis	1	2.5 %	Good	1	2.5 %

Observation:

The outcome of this study in various type of psoriasis showed bright results. Good improvement was observed in Psoriasis vulgaris 18 patients (45 %),Psoriasis vulgaris with Pustular psoriasis 1 patient (2.5 %),Guttate psoriasis 8 patients (20 %),Guttate psoriasis with Pustular psoriasis 1 patient (2.5 %), Psoriasis vulgaris with inverse psoriasis 1 patient (2.5 %). Moderate improvement was observed in Psoriasis vulgaris 6 patients (15 %),Guttate psoriasis 2 patients (5 %) and poor improvement in Psoriasis vulgaris 3 patients (7.5 %).

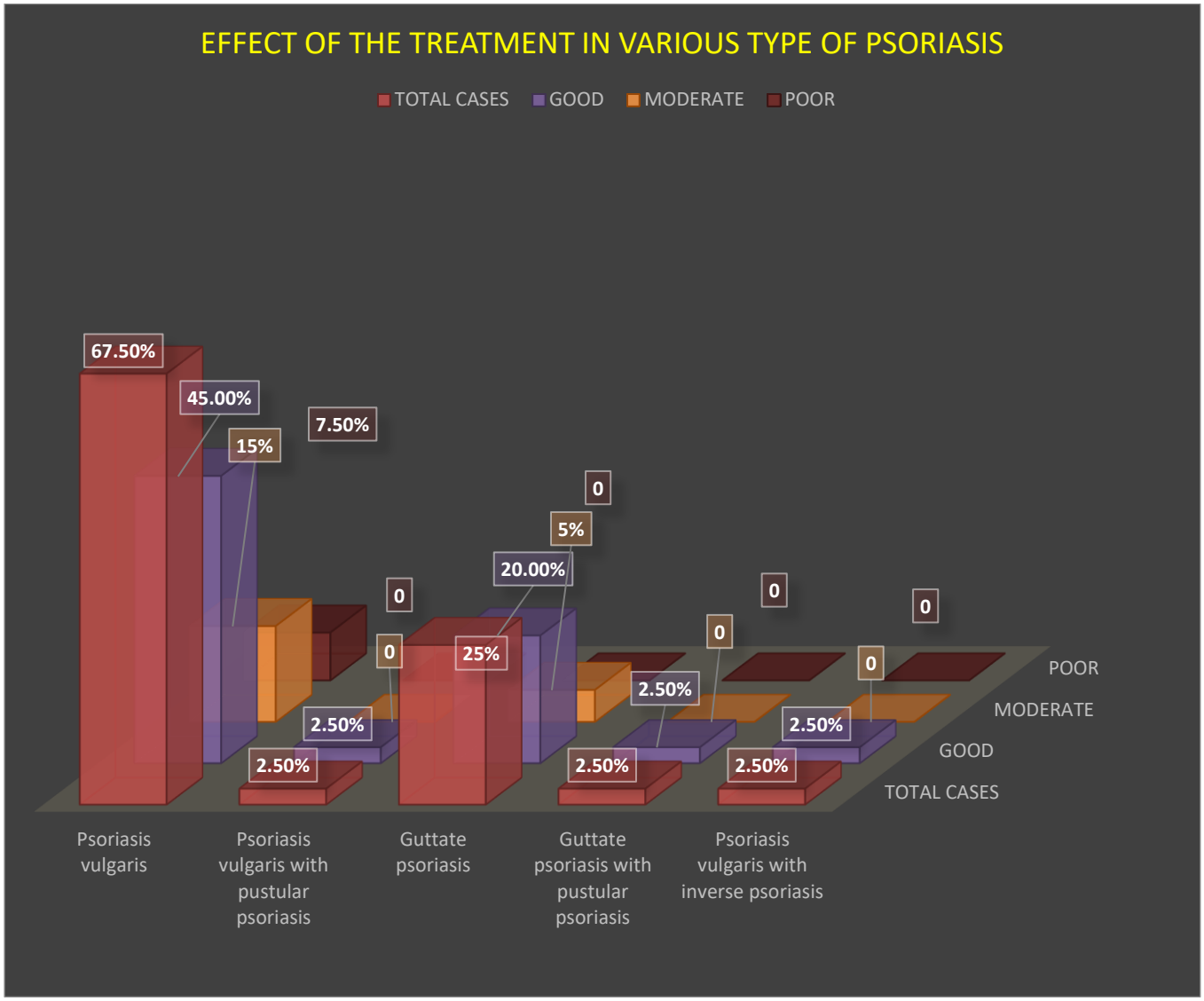


Figure 5.7.30. Effect of Trial Drug in Various Type of KJP

CASE : 1

Figure : 5.7.31 : BT – PASI 46.3
OP NO : K72291 / 21F / Psoriasis Vulgaris With Pustular Psoriasis

49th day (AT) -PASI : 0

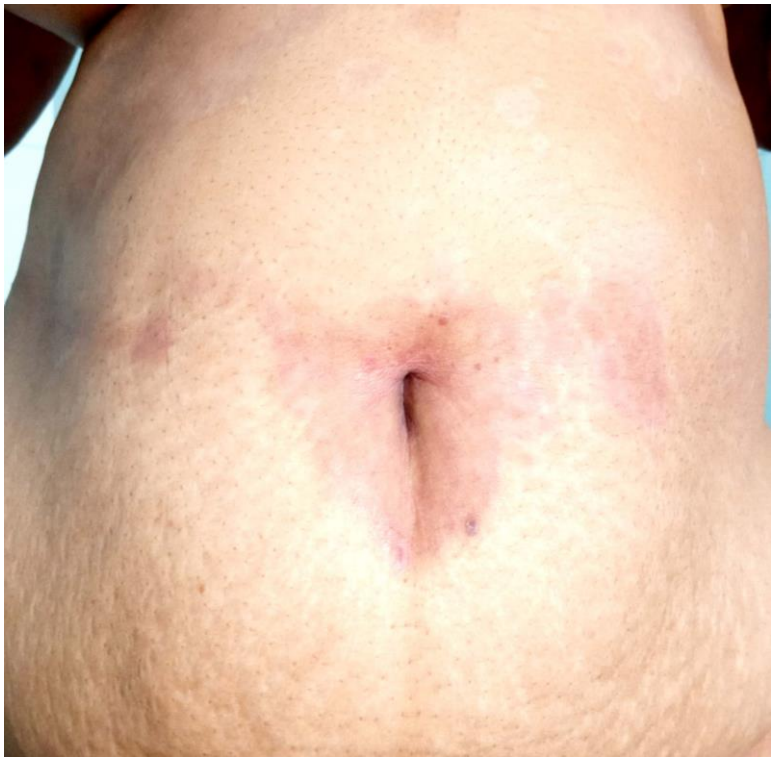
CASE : 2

Figure :5.7.32 : BT – PASI 72
OP NO : F56068 / 60F / Psoriasis Vulgaris With Inverse Psoriasis

1st DAY – PASI : 72

15TH DAY – PASI : 72

49th DAY – PASI : 5



CASE : 3

Figure :5.7.33 : BT – PASI 72
OP NO : K90621 / 36M / Guttate Psoriasis With Pustular Psoriasis

1st DAY : PASI : 72

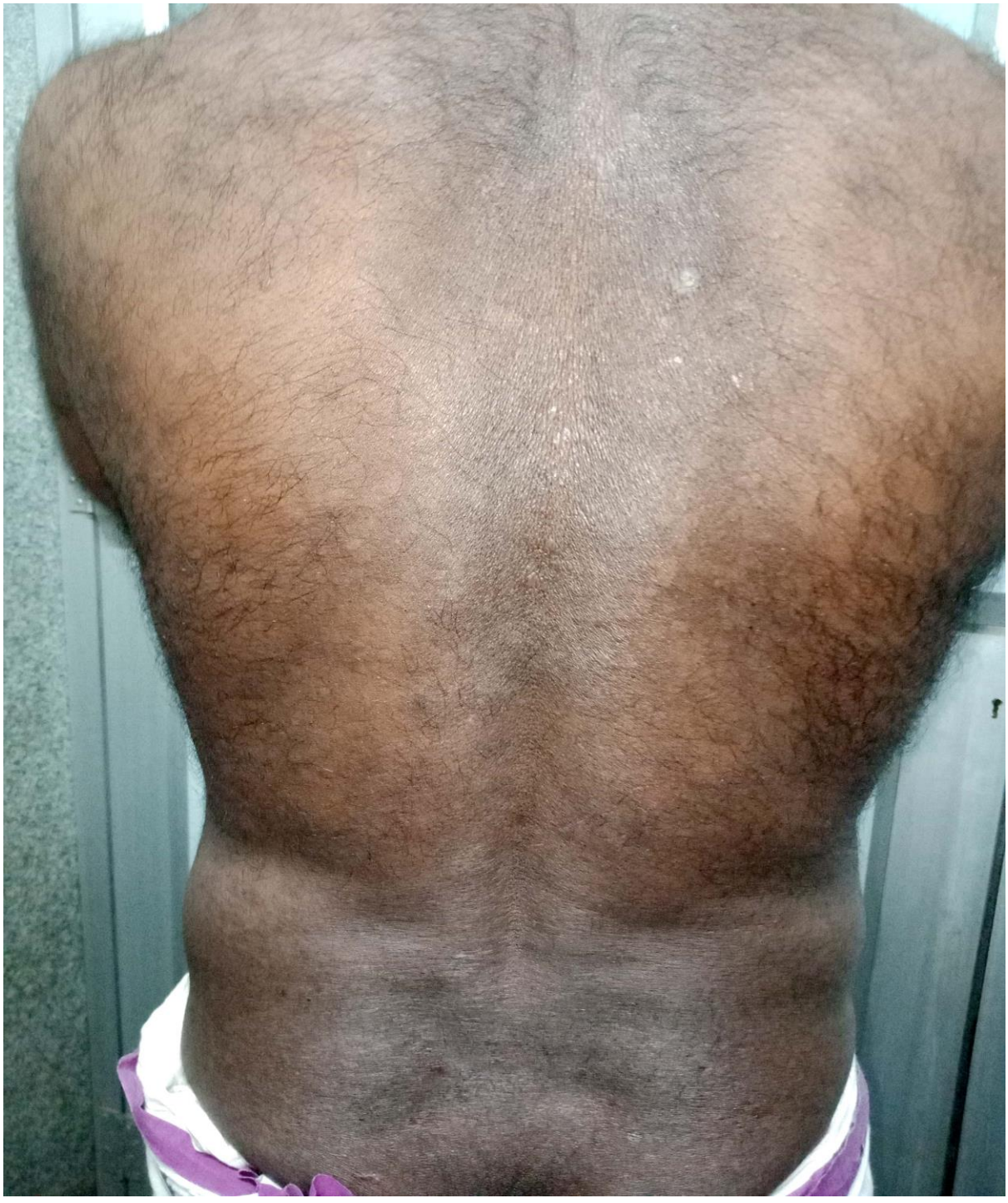
15TH DAY – PASI : 72

49 TH DAY – PASI :3.9

CASE : 4

Figure :5.7.34 : BT – PASI 63.6
OP NO : 1709-18 / 50 M / Psoriasis Vulgaris

49th day – PASI : 0.3



CASE : 5

Figure :5.7.35 : BT – PASI 64.8
OP NO : 0126-19 / 45 M / Psoriasis Vulgaris

49th day – PASI : 0


Wastes)
, Bandage,
nes)
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CASE : 6

Figure : 5.7.36: BT – PASI 72
OP NO : 0221-19 / 33 M / Psoriasis Vulgaris

1st DAY : PASI -72

15TH DAY – PASI : 30.6

49TH DAY – PASI : 0

6.DISCUSSION

Kalanjagapadai (Psoriasis) is important to the clinician because it is common and has treatment implications beyond the care of skin lesions. Psoriasis is a physically,emotionally,socially invalidating multifactorial chronic skin disorder with a significant impact on the patient's quality of life.

The raw drugs of Parangipattai Kudineer were identified and authentication certificate was obtained. Then the raw drugs were purified and PPK was prepared as per the text Pharmacopoeia of hospital of Indian medicine.

"வாதமலாது மேனி கெடாது"

- தேரன் சேகரப்பா

தேகத்தின் ஒளியும் வன்மையும் கெடுவதற்க்கு வளிக்குற்றமே முதற்காரணமாகும்.

As per siddha system taste and potency of the drug was important to act on regulate the humors. Both trail drug has mostly bitter,spicy,sweet taste and hot potency.Basically hot potency mitigate vatham humor and alliviate the kaba disease, allergies. Bitter taste act on toxic substance from the body and healing of skin diseases(Kuttam). Spicy taste act on toxic substance from the body and healing of skin diseases,wounds (Kuttam).Sweet taste act on vatha pitham humor eliminates the pitham and toxic substance and give the strength to udalthathukkal (body constituents) and glowing of skin. Hence these compounds possess promising act against *Kuttam (Kalanjgapadai*).

Analytical specifications :

Solid- Crude raw Material of PPK was greenish brown in colour and Decoction- Water Extraction of PPK was reddish brown in colour.Due to pH value of 4.5 of PPK and it is available in intestine without getting affected.

This formulation satisfy the Pharmacopoeial standards and as per the WHO Guidelines. Microscopic observation of the particle size analysis reveals that the average particle size of the PPK sample was found to be 175.7 ± 71.8 µm.

The drug is free of microbial contamination, pesticide residues and aflatoxins. The heavy metals were not detected (arsenic, mercury, cadmium) except lead which was within the AYUSH & WHO permissible limit. It was may be evident of drug's ingredients had lead content herb as per followed Siddha literature,

*"**சீந்தில்** விழுதி சிறுபீளை வெள்ளறுகும்*

*ஏந்திழையீ **ரீயமுலி"***

- குணப்பாடம்;தாது சீவ வகுப்பு

One of the drug's ingredients was *Tinospora cordifolia* which was lead content herb. HPTLC finger printing analysis of the sample PKC reveals the presence of six prominent peaks corresponds to presence of six versatile phyto-components present with in it. Rf value of the peaks ranges from 0.05 to 0.71. Further the peak 2 and 6 occupies the major percentage of area of 37.55 and 36.53 % which denotes the abundant existence of such compound. Followed by this peak 1 and 3 occupies the percentage area of 18.18 and 3.11 %.

Preliminary Phytochemical Screening :

Flavonoids, Phenolic Compounds and Quinones, Saponins,Carbohydrates were presnt in this drug.Their presence indicates antioxidant, antimicrobial, anti-allergic, antifungal and anti-inflammatory properties of the drug. Saponins has phytosterol of sarsasapogenin which it is act as steroid.

Chemical Analysis :

Chloride and Carbonate (acid base equilibrium,regulate fluid balance), Phosphate (Regulate Parathyroid hormone,Vitamin D,Acid base balance). Iron (Effective immunocompetence), Zinc (Maintain immune status , Anti-inflammatory, Inhibit keratinocytes, modulates production of TNF-α,IL-6) ,Alkaloids (Antifungal.Antimicrobial, antioxidant), Tannic acid (Aniseptic,antiallergy,antidote) and oxyquinole (Antimicrobial) epinephrine (anaphylaxsis,vasoconstricor) and pyro catechol (Antioxidant) were presnt in this drug.

In -Vitro Pharmacological Screening of PPK (Internal drug) :

In-vitro pharmacological activities has been done for PPK drug and this drug had activities of ***anti-inflammatory (protein denaturation assay), immunomodulatory, anti-proliferative (HaCaT keratinocyte cell line)***

In docking analysis on PPK (Internal drug) :

Amino acid Residue Interaction of Lead and Standard against IL- 6 – PDB 1P9M :

Out of six compound's Berberine has 2 interactions similar to that of the standard Tacrolimus. Other compounds such as Anisaldehyde , Kaempferol and Nimbolide has one interaction similar to that of the standard. Hence these compounds possess promising IL-6 inhibition activity.

Amino acid Residue Interaction of Lead and Standard against TNF-alpha (2AZ5) :

Out of six compound's Picein and Anisaldehyde has 4 interactions similar to that of the standard Tacrolimus. Other compounds such as Berberine, Kaempferol, Protocatechuic acid and Nimbolide has three interaction similar to that of the standard. Hence these compounds possess promising TNF- alpha inhibition activity.

Amino acid Residue Interaction of Lead and Standard against Nitric Oxide Synthase :

Out of six compound's Picein and Anisaldehyde has 4 interactions similar to that of the standard Tacrolimus. Other compounds such as Berberine, Kaempferol and Nimbolide has three interaction similar to that of the standard. Hence these compounds possess promising Nitric oxide synthase enzyme inhibition activity.

In -Vitro Pharmacological Screening of Sivappu thylam (External drug) :

In-vitro pharmacological activities has been done for external medicine of Sivappu thylam and this drug had activities of ***anti-inflammatory*** property in protein denaturation assay.

Toxicity study :

The Acute and 28 days repeated oral toxicity studies did not show any toxic effects in the animals.

Clinical study:

For this study, 40 patients were selected and 20 patients were treated in the OPD, 20 patients were treated in the IPD at department of Sirappu Maruthuvam, in Ayothidoss Pandithar Hospital of National Institute of Siddha, Tambaram Sanatorium, Chennai – 600 047.

Group I : Trail drug without yogam in (20) OPD patients.

Group II : Trail drug with yogam in (20) IPD patients.

First day :

Agathiyar kulambu with 200mg with 30ml leaf juice of Sangankuppi (*Azima tetracantha*) quantity was administered at early morning as purgative (*Kazhichal* Medicine) before starting the treatment for restore equilibrium of uyirthathus.

Second day :

Oil bath with *Arakku thylam* has taken at early morning for restore equilibrium of udalthathus.

Third day onwards from Sunday / Tuesday / Thursday for 48 days :

Internal Medicine: *Parangipattai Kudineer,* three times a day before food.

External Medicine: *Sivappu thylam*

Advice for method of topical medicine :

Oil applied in psoriatic lesion by cotton for 4 hrs at 1pm to 5pm and take sunbath at 4pm to 5.30pm thereafter bath with warmwater used by greengram powder.

Benefit of sunbath:

Exposure to sunlight is thought to increase the brain's release of hormone called serotonin.Serotonin is help a patient feel calm and focus and reduced depression mood. Sunlight induced synthesis of Vitamin D.Vit D might represent a key modulator of immune and inflammation mechanisms.

OPD patients are requested to visit the hospital once in 7 days. In each and every visit clinical assessment and prognosis were recorded. For IPD patients the clinical assessment and prognosis were recorded daily.

In Siddha investigation of Envagai Thervu will be evaluvate before and after the treatment for 40 patients. Nei Kuri will be evaluvate 0^{th} day,15^{th} day,49^{th} day of the treatment for opd and IPD patients. Manikadai Nool will be measure before treatment for 40 patients.

In Moderen ; Laboratory investigations were done before and after the trial. There were no variations in hepatic, renal and other parameters. For IPD patients, who are not in a position to stay in the hospital for a long time are advised to attend the OPD for further follow-up. At the end of the trial, the patients are advised to follow-up for 2 months in visit the OPD .

Based on various criteria, the data were collected and tabulated. The criteria were family history, sex predominance, age distribution, occupation, dietary habits and incidence of the disease with reference to thinai, seasonal variation, clinical manifestations and assessment of the improvement in the prognosis of the disease with the trial drug.

40 patients of both genders were recruited for this study. Among the 40 cases, 30 (75%) were males and 10 (25%) were females. Generally the prevalance Kalanjagapadai may observed in males more than female during study period of kaarkalam (mid augest to mid october), koothirkalam (mid october to mid december),munpanikalam (mid december to mid february).

Out of 40 cases, 27.5% patients were between 18 to 30 years old, 25% patients between 31 to 40 years, 25% patients between 41 to 50 years, (22.5%) patients between 51 and 60 years,. Kalanjagapadai can appear at birth as well in very old age. In this present study, considerable number of patients were reported (11 patients) between the ages of 18-30 among study sample.There were no differences in age in the onset of psoriasis between men and women with psoriasis.

Among 40 cases, 15 in Vaatha kaalam (1-33 Years) and the remaining 25 patients reported in Pitha kaalam (34-66 Years).The age group between 18 to 45 years experienced more frequent problems related to occupation, finance and work-related stresses as a result of their psoriasis.

Out of 40 patients reported, the high prevalence of psoriasis was in working people field work with physical exertion 70%, field work with intellectual job 17.5%, house-wife 10%, and students 2.5%. The results did not declare psoriasis as an occupational related disease.

Family history was a risk factor for psoriasis. In this present study 15% of patients had family history.85% of the patients showed negative family history.Remissions and relapse of this disease are quite common. 90% of patients had the previous history of remission and relapse.

Among the 40 patients selected for this study, 85% were non-vegetarian. In the text ***Yugimuni 800,*** non-vegetarian diet is mentioned as one of the causes for Kuttam. In this present study the above cause has been proved.

Out of 40 patients, 7.5% of patients had tobacco chewing habits,Smoking and alcohol 15 % and 10% of patients had alcohol consuming habits.There is a strong association between smoking, alcohol consuming, tobacco chewing habits and psoriasis lesions. In this present study it has been proved that risk factors for psoriasis are smoking, alcohol, diet and stressful life events.

In this present study, 7.5% of the patients were from Marutham (Fertile Land), 17.5% of the patients were from Kurinji (Hill Area), 20% of the patients were from Mullai (Forest Area) and the remaining 55% from Neithal (Coastal Area).Considerable numbers of patients were reported from neithal. According to Siddha literature coastal area is more prone to skin diseases.

Patient enrollement period was various seasons especially Kaar kaalam,Koothir kaalam,Munpanikaalam only and didn't enroll of patient in other seasons. In this study, the highest number of patients reported in (45%) Munpani kaalam.

In this study, The maximum numbers of patients had Pitha udal (37.5 %) and 100 % of the patients had Rajo Gunam.

Out of 40 patients, 35 % of the patients were suffering with during of the illness for 1-3 years.

In Poripulan ; Before treatment mei were found to be affected in all the 40 patients.. After treatment mei were found to be affected in 27.5% of patients.

In Kanmendhiriyam ; Before treatment eruvai were found to be affected in one patients.. After treatment eruvai were found to be no abnormalities.

In kosam ; Before treatment were found to be affected 7.5% patients in annamayakosam, 2.5% in pranamayakosam,100% in manomayakosam. After treatment were found to be affected 2.5% in pranamayakosam,32.5% in manomayakosam.

In Vatham ; Before treatment Udhanan,Samanan and Viyanan were found to be affected in all the 100% patients.Pranan was found to be in 2.5% of patients, Abanan was found to be in 2.5% of patients, Kirukaran was found to be in 7.5% of patients, Devathathan was found to be affected in 22.5% of patients. After treatment Udhanan,Samanan and Viyanan were found to be affected in 40% of patients. Pranan was found to be in 2.5% of patients.

In Pitham ; Before treatment Ranjagapitham,Prasagapitham was affected in all the cases and anarpitham was affected in 7.5% patients. After treatment Ranjagapitham,Prasagapitham was affected in 27.5% patients.

In Kabam ; Before treatment kiledhagam was affected in 7.5%.Before and after treatment Avalambagam thee was affected in one case.

In Udal Kattukkal ; Before treatment ; Saaram and Seneer, Oon were affected in 100% of cases. After treatments Saaram, Seneer, Oon were affected in 27.5% of cases.

In Envagai thervugal, before treatment Niram and Sparisam were found affected in all the 40 cases, Malam was found affected in 1 cases. The Naadinadai seen in Kalanjagapadai patients were Vaathapitham 5%, Pithavaatham 62.5 %, Pithakabam 17.5 %, Kabapitham 2.5%, Vathakabam 12.5%. After treatment Niram,sparisam affected in 11 cases, The Naadi nadai seen in Kalanjagapadai patients were Vaathapitham 77.5%, Pithavaatham 20 %,
Pitha kabam 2.5 %.

On Neerkuri ; Before treatment the majority of patients had *Citrus aurantium* fruit colour (47.5%) and wild *citrus medica* fruit colour 37.5%, Hey soaked rain water colour 12.5%,Reddish yellow colour 2.5%.After treatmentthe majority of patients had *Citrus aurantium* fruit colour (40%) and wild *citrus medica* fruit colour 5%, Hey soaked rain water colour 55%.

On Neikuri :

On 1st day the patients had Kabam (Pearl) Neikuri pattern (55%), VP Neikuri pattern (5%),PP Neikuri pattern (5%), PV Neikuri pattern (2.5%), Mukkuttram Neikuri pattern(2.5%) and Severe Kabam (Saladaikan pattern) (30%).

On 15th day the patients had Kabam (Pearl) Neikuri pattern (37.5%),Pitham Neikuri pattern(12.5%) , VP Neikuri pattern (12.5%), PV Neikuri pattern (5%),VK Neikuri pattern (2.5%),Mukkuttram Neikuri pattern (2.5%) and Severe Kabam (Saladaikan pattern) (27.5%).

On 49th day the patients had Vatham Neikuri pattern (5%), Pitham Neikuri pattern (30%),Kabam (Pearl) Neikuri pattern (12.5%), VP Neikuri pattern (2.5%),PV Neikuri pattern (25%),PK Neikuri pattern (10%),Mukkuttram Neikuri pattern(2.5%) and Severe Kabam (Saladaikan pattern) (12.5%).By this study proved to assessment of prognosis of the treatment.

In *Mankadainool*, before treatment the majority of patients had 8 ½ finger breadth (72.5%) .

In this study, 45% of patients started medicine on Sunday, 27.5% of patients started medicine on Tuesday , 27.5% of patients started medicine on Thursday as per Siddha literature. The majority of patient had medicine on Sunday with good improvement.So from this result medicine started on Sunday was *Uthamam* as per Siddha literature.

The haematological and biochemical parameters were tested for the patients treated with PPK and it was found that there was no major difference both before and after treatment. This vouches for the safety of the trial drug administered as the values were well within the normal limits.

Before treatment all the patients had the clinical features of erythema, scaling, itching, Auspitz sign, Candle grease sign and 12.5 % of cases had Fissure, 7.5 % of cases had pustule. After treatment 42.5% of cases had erythema, 30% of cases had scaling, 1.5% of cases had itching, 15% of cases had Auspitz sign, 30% of cases had Candle grease sign. 92.5% of cases had irregular shape of lesion.

The most common discomfort encountered by the patients who had Psoriasis was Itching and scaling. 40 patients out of 40 (100%) had this symptom and the test drug PPK corrected symptom of itching in 87.5% of the patients and corrected symptoms of scaling in 70 % of patients. The symptom of erythema was found all patients (100%). This was cleared in most of the patients (57.5%) who had this complaint.The symptom of fissure (12.5%) , pustule (7.5%) was found in the patients. This was cleared all patients who had fissure and pustule complaint.The most common signs in the patients who had Psoriasis was auspitz sign and candle grease sign. 40 patients out of 40 (100%) had this signs and the test drug PPK clear the sign of auspitz sign in 85% of the patients and candle grease sign in 70% of the patients.

Psoriasis is a disease that impacts the quality of life of patients, particularly in its severe clinical forms. Quality of life score in before treatment score 21-30 in 40 patients. After treatment score 0-1 in 19 patients, score 2-5 in 11 patients, score 6-10 in 1 patients, and score 11-20 in 7 patient. Score 21-30 in 2 patients.

Inference of the treatment assessment response with PASI Score :

Group I was shown 42.07±6.98 on first day (BT) and it was 12.39±5.08 on it 49^{th} day (AT).Till 15^{th} , there is a gradually increase of PASI score i.e. upto 44.43±7.11 and after 15^{th} day day of the treatment, the PASI score declines to 12.39±5.08 (49^{th} day)

Group II was shown 43.46±7.77 on first day (BT) and it was 4.22±2.16 on it 49^{th} day (AT).Till 49^{th} day, there is a gradually declines of PASI score.

Both group (all patient) was shown 42.76±7.30 on first day (BT) and it was 8.3±4.27 on it 49^{th} day (AT).Till 15^{th} day, there is a gradually increase of PASI score i.e. upto 43.67±6.84 and after 15^{th} day of the treatment, the PASI score declines to 8.3±4.27 (49^{th} day).

Paired Sample Statistics (mean± SEM PASI Score Before Treatment and After Treatment) :

Group I was shown 42.07±6.98 and 12.39±5.08 respectively which is statistically very significant ($t = 3.438$, $p < 0.0014$).

Group II was shown 43.46±7.77 and 4.22±2.16 respectively which is statistically extremely significant ($t = 4.866$, <0.0001).

Observation of assessment of the treatment response with PASI Score :

According to above the inferences ; Initially the symptoms of psoriasis may be aggravated and then gradually declines by the trail drug.

As per paired sample statistics , Group II (with yogam) was shown excellent outcome of the treatment greaterthan Group I (without yogam).

Outcome :

The outcome of this study showed promising results. In group I : Good improvement was observed in 13 patients (65%), moderate improvement in 4 patients (20%), and poor improvement in 3 (7.5%) cases. In group II : Good improvement was observed in 16 patients (80%), moderate improvement in 4 patients (20%).

Effect of trial drug in various type of KJP :

The outcome of this study in various type of psoriasis showed bright results. Good improvement was observed inPsoriasis vulgaris 18 patients (45 %),Psoriasis vulgaris with Pustular psoriasis 1 patient (2.5 %),Guttate psoriasis 8 patients (20 %),Guttate psoriasis with Pustular psoriasis 1 patient (2.5 %), Psoriasis vulgaris with inverse psoriasis 1 patient (2.5 %). Moderate improvement was observed in Psoriasis vulgaris 6 patients (15 %),Guttate psoriasis 2 patients (5 %).and poor improvement in Psoriasis vulgaris 3 patients (7.5 %).

7.SUMMARY

- ✶ The raw drugs of PPK were identified and authentication certificate was obtained.
- ✶ The analytical specifications of the prepared drug revealed that it was in the standard quality.
- ✶ HPTLC finger printing analysis of the sample PKC reveals the presence of six prominent peaks corresponds to presence of six versatile phyto-components present with in it. Rf value of the peaks ranges from 0.05 to 0.71. Further the peak 2 and 6 occupies the major percentage of area of 37.55 and 36.53 % which denotes the abundant existence of such compound. Followed by this peak 1 and 3 occupies the percentage area of 18.18 and 3.11 %.
- ✶ The toxic elements like Mercury, Arsenic and Cadmium are not detected. Further the results show the presence of Lead and Arsenic and cadmium at 1.185 and 0.460 ppmlevel.The reported heavy metal seems very low when compare to the allowed within the AYUSH & WHO permissible limit.
- ✶ In-vitro pharmacological activities has been done for PPK drug and this drug had activities of anti-inflammatory (protein denaturation assay), immunomodulatory, anti-proliferative (HaCaT keratinocyte cell line)
- ✶ In docking analysis on PPK : PPK compounds possess promising IL-6 inhibition activity, TNF- alpha inhibition activity, Nitric oxide synthase enzyme inhibition activity.
- ✶ In-vitro pharmacological activities has been done for external medicine of Sivappu thylam and this drug had activities of anti-inflammatory property in protein denaturation assay.
- ✶ The safety profile study has been approved by **IAEC of NIS.[Date of IAEC Approval & its number: NIS/IAEC VI /24/04/2018/09].**
- ✶ The study shows that PPK did not produce any toxic effect at dose of 2000 mg/kg. So No-Observed-Adverse-Effect-Level (NOAEL) of PPK is 2000 mg/kg.
- ✶ NOAEL of PPK was found to be greater than 27 mg/kg/p.o/day in rats.
- ✶ This study has been approved by **IEC of NIS.[Date of IEC Approval & its number: NIS/13-IEC/2017-1-08/22-11-2017].**
- ✶ The disease Kalanjagapadai was taken for the clinical study with Parangipattai Kudineer (Internally), Sivappu thylam(Externally) and 40 cases were selected based on the approved protocol.

- Group I : Trail drug without yogam in (20) OPD patients.
- Group II : Trail drug with yogam in (20) IPD patients.

✶ Animal studies were done after obtaining approval from the Animal Ethical Committee (IAEC). Hence the study was safely executed on patients and there was no adverse drug reactions noted during the study period.

✶ The detailed study on Kalanjagapadai with reference to its etiology, pathogenesis, investigations, clinical features, diagnosis and treatment with trial drug was done.

Inference of the treatment assessment response with PASI Score :

Group I was shown 42.07±6.98 on first day (BT) and it was 12.39±5.08 on it 49th day (AT).Till 15th , there is a gradually increase of PASI score i.e. upto 44.43±7.11 and after 15th day day of the treatment, the PASI score declines to 12.39±5.08 (49th day)

Group II was shown 43.46±7.77 on first day (BT) and it was 4.22±2.16 on it 49th day (AT).Till 49th day, there is a gradually declines of PASI score.

Both group (all patient) was shown 42.76±7.30 on first day (BT) and it was 8.3±4.27 on it 49th day (AT).Till 15th day, there is a gradually increase of PASI score i.e. upto 43.67±6.84 and after 15th day of the treatment, the PASI score declines to 8.3±4.27 (49th day).

Paired Sample Statistics (mean± SEM PASI Score Before Treatment and After Treatment) :

Group I was shown 42.07±6.98 and 12.39±5.08 respectively which is statistically very significant ($t = 3.438$, $p < 0.0014$).

Group II was shown 43.46±7.77 and 4.22±2.16 respectively which is statistically extremely significant ($t = 4.866$, < 0.0001).

Observation of assessment of the treatment response with PASI Score :

According to above the inferences ; Initially the symptoms of psoriasis may be become aggravated and then gradually declines by the trail drug.

As per paired sample statistics , Group II (with yogam) was shown excellent outcome of the treatment greaterthan Group I (without yogam).

Outcome :

The outcome of this study showed promising results. In group I : Good improvement was observed in 13 patients (65%), moderate improvement in 4 patients (20%), and poor improvement in 3 (7.5%) cases. In group II : Good improvement was observed in 16 patients (80%), moderate improvement in 4 patients (20%).

Effect of trial drug in various type of KJP :

The outcome of this study in various type of psoriasis showed bright results. Good improvement was observed inPsoriasis vulgaris 18 patients (45 %),Psoriasis vulgaris with Pustular psoriasis 1 patient (2.5 %),Guttate psoriasis 8 patients (20 %),Guttate psoriasis with Pustular psoriasis 1 patient (2.5 %), Psoriasis vulgaris with inverse psoriasis 1 patient (2.5 %). Moderate improvement was observed in Psoriasis vulgaris 6 patients (15 %),Guttate psoriasis 2 patients (5 %).and poor improvement in Psoriasis vulgaris 3 patients (7.5 %).

In this study, no adverse events were observed during the course of the treatment. At the end of the study, all the patients were advised to attend out-patient department of Sirappu Maruthuvam of NIS for further follow-up and also for *Niraivu* (Restoration) *and Kaappu* (Prevention).

8.CONCLUSION

The poly herbal formulation *Parangipattai Kudineer (PPK)* exhibited no toxicity on short term administration.

PPK drug had activities of In-vitro; anti-inflammatory (protein denaturation assay), In-vitro; immunomodulatory, In-vitro; anti-proliferative (HaCaT keratinocyte cell line) and in docking analysis on PPK : PPK compounds possess promising IL-6 inhibition activity, TNF-alpha inhibition activity, Nitric oxide synthase enzyme inhibition activity.

Sivappu thylam drug had activities of In-vitro; anti-inflammatory property in protein denaturation assay.

The present clinical study confirms the efficacy and safety of the trial drug *"Parangipattai Kudineer* (Internally) and *Sivappu thylam* (Externally)" which is Siddha poly herbal formulation. It was found to be highly effective on Kalanjagappadai patients in reducing clinical signs and symptoms like itching, scaling and erythema.

The outcome of this study showed promising results. In group I : Good improvement was observed in 13 patients (65%), moderate improvement in 4 patients (20%), and poor improvement in 3 (7.5%) cases. In group II : Good improvement was observed in 16 patients (80%), moderate improvement in 4 patients (20%).

From the above results, the trail drug "*Parangipattai Kudineer* (Internally) and *Sivappu thylam* (Externally)" was responded well with Yogam therapy more than without yogam in the treatment of *Kalanjagappadai*.

As a conclusion it can be stated that the Siddha herbal formulation *PPK & ST* can be used as a safe and extremely efficacious drug with Yogam therapy more than without yogam towards the management of *Kalanjagapadai* which takes a huge toll of inducing psychological stress and impact on the cosmetic purposes.

PASI SCORE

S.NO	OP NO	AGE/SEX	GROUP I PASI SCORE								PASI Score	Result
			1st Day	8th Day	15th Day	22nd Day	29th Day	36th Day	41th Day	48th Day		
1	K72291	21F	46.3	52.8	47.4	35	34.8	31.2	12.9	0	PASI-100%	Good
2	K52043	36M	39	35	24.7	24.7	24.7	24.7	16.3	16.3	PASI-50%	Moderate
3	K73392	49M	47	47	28.7	23.9	23.9	13.6	3.4	0.3	PASI-90%	Good
4	K73775	35M	51.3	51.3	47	47	37	30.8	27.2	27.2	PASI-50%	Moderate
5	K12822	42M	57.1	57.1	49.7	49.7	41	41	24	24	PASI-50%	Moderate
6	K76317	30F	45.3	45.3	50.1	38.7	32.3	22.1	22.1	12	PASI-75%	Good
7	K55057	41M	34.2	34.2	37.2	37.2	25.3	23.5	23.5	22.6	PASI-25%	Poor
8	F56068	60F	72	72	72	64.4	64.4	30.3	15.2	5	PASI-90%	Good
9	K90621	36M	72	72	72	49.3	34.8	34.8	17.7	3.9	PASI-90%	Good
10	H64353	27F	34.2	63.6	63.6	51.2	32.8	14.9	3	0.9	PASI-90%	Good
11	K96821	24F	31.9	31.9	56.5	41.5	23.6	20.4	15	7.8	PASI-90%	Good
12	K26618	32M	32.4	32.4	32.4	28	28	16.9	16.9	2.4	PASI-90%	Good
13	K98126	48M	21	21	21	13.5	12.9	8.5	3.9	3.3	PASI-90%	Good
14	L06124	46M	56	56	56	33	30.3	25.3	22.4	15.4	PASI-75%	Good
15	G75597	42M	52.8	52.8	52.8	52.8	50.4	48.4	43.6	43.6	PASI-10%	Poor
16	I53688	51M	48.6	48.6	48.6	42.6	36.6	18	17.2	17.2	PASI-50%	Moderate
17	L10109	60M	25.2	25.2	25.2	25.2	23.3	23.3	22.4	22.4	PASI-1%	Poor
18	L14103	32F	19.2	19.2	19.2	19.2	13	13	5.9	3.9	PASI-90%	Good
19	L17159	35F	19.5	19.5	48.1	48.1	40	34.3	22.4	13.2	PASI-75%	Good
20	K71327	52M	36.4	36.4	36.4	30.1	30.1	26.2	8.1	6.3	PASI-90%	Good

S.NO	IP NO	AGE/SEX	GROUP II PASI SCORE								PASI Score	RESULT
			1st Day	8th Day	15th Day	22nd Day	29th Day	36th Day	41th Day	48th Day		
1	1361-18	27M	70	70	43.8	43.5	35.1	28.7	0.3	0.3	PASI-90%	Good
2	1396-18	32F	66	66	64	64	45.5	45.5	22.3	16.9	PASI-50%	Moderate
3	1422-18	50M	44.3	44.3	35.1	35.1	33.6	33.3	20.9	10.7	PASI-75%	Good
4	1456-18	43M	48	48	42.6	17.7	16.5	1.6	0	0	PASI-100%	Good
5	1524-18	47F	42.2	42.2	42.2	35.9	18.7	8.3	3.1	3.1	PASI-90%	Good
6	1526-18	21M	28	28	53.9	53.9	39.2	22.3	12.9	3.3	PASI-90%	Good
7	1557-18	60F	41.8	41.8	41.8	32.7	22.8	14.4	6.9	6	PASI-75%	Good
8	1709-18	50M	35.1	35.1	63.6	63.6	49	31.7	9	0.3	PASI-90%	Good
9	1720-18	26M	22.2	22.2	22.2	20.1	17	7.3	1.1	0	PASI-100%	Good
10	1762-18	26M	17.8	17.8	17.8	13.2	8.7	6	3.9	0.4	PASI-90%	Good
11	0033-19	34M	32.1	32.1	32.1	26.1	22.1	15.1	3.4	0.4	PASI-90%	Good
12	0092-19	24M	53.4	53.4	53.4	36.5	25.4	21	16.8	11.6	PASI-50%	Moderate
13	0054-19	25M	51.6	51.6	50.1	33.9	37.3	25.6	15.3	8.3	PASI-75%	Moderate
14	0055-19	60M	48	48	66	66	47.8	42.6	17.8	2.4	PASI-90%	Good
15	0106-19	24M	19.8	19.8	36	36	30.6	19.2	13.7	7.3	PASI-75%	Moderate
16	0126-19	45M	64.8	64.8	44.8	23.2	3	0	0	0	PASI-0%	Good
17	0136-19	50M	28	28	28	26.6	16.2	16.2	6.3	1.1	PASI-90%	Good
18	0174-19	40M	60.6	60.6	66.6	52.8	29.5	28.2	5	5	PASI-75%	Good
19	0181-19	54M	23.4	23.4	23.4	17.2	12.6	10	7.2	7.2	PASI-75%	Good
20	0221-19	33M	72	72	30.6	19.7	10.5	6.6	5.8	0	PASI-100%	Good

INVESTIGATIONS

(BEFORE AND AFTER TREATMENT)

S.No	Hb (gm/dl)		TOTAL RBC COUNT (million/cu.mm)		ESR (mm/hour)				TOTAL WBC (cells/cu.mm)		PLATELETS (lak/cu.mm)	
					1/2hr		1hr					
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P1	14.2	14.4	4.4	4.5	22	19	30	25	7700	8200	1.7	1.8
P2	14.8	14.5	5.6	5.6	32	20	64	44	6300	5800	2.7	2.3
P3	16.5	15.5	4.9	4.9	40	20	51	40	9300	6000	2.8	2.3
P4	15.8	15	4.5	5.2	14	3	20	10	7300	6600	1.4	1.4
P5	14.8	15	5.2	5.5	14	6	18	10	6400	6700	2.5	2.5
P6	12.4	13	4.2	4.4	20	22	40	39	9200	9300	2.5	2.7
P7	13.9	14.1	3.8	3.7	10	6	22	12	9800	7600	3.9	3.1
P8	12.6	13.1	4.7	4.8	20	6	40	12	6400	5600	3.4	3.1
P9	13.5	14.2	4.8	4.8	16	10	34	22	12800	10400	4.3	4.3
P10	10.8	10.9	4.1	4.2	16	20	32	42	5900	6600	2.2	2.1
P11	11.5	12	4.5	4.6	10	16	20	30	12100	10600	3.2	3.3
P12	12	13	4.6	4.6	14	12	22	26	7700	6600	2.7	2.2
P13	15.6	15.3	4.8	4.6	14	6	18	12	8900	8400	2.3	2.1
P14	12.4	13	4.2	4.3	24	18	50	26	9600	9400	2.4	2.1
P15	15.7	15.2	5.5	5.5	14	10	30	22	8100	8800	3.1	3.4
P16	14.6	13.6	4.9	4.3	6	6	12	12	9900	8300	3	2.8
P17	15.8	14.8	5.8	5.4	16	40	32	82	10100	8200	2	2.4
P18	13.2	14	4.5	4.7	12	6	24	12	7000	8100	2.8	2.9
P19	13.6	13.7	4.6	4.8	6	14	12	20	6400	8400	3.7	3.8
P20	10.3	9.8	4.3	3.8	30	22	62	46	7600	7000	3.9	3.6

S.No	Hb (gm/dl)		TOTAL RBC COUNT (million/cu.mm)		ESR (mm/hour)				TOTAL WBC (cells/cu.mm)		PLATELETS (lak/cu.mm)	
					1/2hr		1hr					
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P21	12	14.2	4.7	5.1	22	6	50	12	4000	5200	2.9	2.7
P22	9.8	10.6	4.4	5	20	18	40	36	*6600*	6700	*4.2*	4.3
P23	15.1	14.7	4.6	4.6	4	4	10	10	*6200*	6100	*2.4*	2.6
P24	15.5	16	4.6	4.6	4	6	10	12	*6500*	6700	*3*	3.5
P25	10.8	11.7	4.8	5.2	12	8	24	16	*5400*	5600	*2.7*	2.9
P26	16.2	14.9	5.6	5.1	2	4	6	8	*5100*	7300	*3.2*	3.4
P27	11.6	13.1	4.2	4.8	20	10	40	22	*7400*	6600	*3*	3.2
P28	15.1	15.4	5.2	5.4	12	6	24	12	*9700*	7600	*2.9*	3.3
P29	14.9	15.1	5.5	5.5	12	12	24	26	*5100*	4800	*2.6*	2.4
P30	16.4	15.5	5.6	5.4	12	14	24	28	*4500*	4300	*1.9*	2
P31	15.3	15.2	4.6	4.5	12	6	24	12	*7600*	8600	*2.5*	2.8
P32	15.3	14.9	4.6	5.3	12	6	14	12	*7600*	7200	*2.8*	2.5
P33	13	14.7	4.4	4.9	20	7	40	14	*7900*	5400	*2.3*	2
P34	13.3	11.9	4.1	3.5	10	8	20	16	*5700*	5500	*2.6*	2.1
P35	14.1	13	6.4	5.8	8	7	16	14	*11900*	8500	*3.6*	2.7
P36	14.9	13.8	4.6	4.4	6	6	12	12	*5700*	9100	*3.3*	3.9
P37	14.6	13.9	3.8	3.8	8	7	16	14	*6900*	8100	*2*	1.9
P38	14.8	14.4	5.2	5	6	8	12	16	*8100*	7900	*3.3*	2.9
P39	13.5	13.5	4.7	4.6	30	18	60	36	*8100*	7200	*3.5*	3.5
P40	16.5	16.1	5.2	5.2	8	8	18	18	*11400*	9100	*2.1*	2.1

S. No.	Total Bilirubin		Direct Bilirubin		Indirect Bilirubin		SGOT (IU/L)		SGPT (IU/L)		Alkaline Phosphatase	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P1	1.2	0.8	0.5	0.4	0.7	0.4	19	29	8	21	57	41
P2	0.5	0.8	0.2	0.3	0.3	0.5	17	15	3	3	191	150
P3	1.1	1.4	0.4	0.5	0.7	0.9	45	30	63	22	65	48
P4	0.5	0.5	0.2	0.1	0.3	0.2	14	18	17	20	81	82
P5	0.5	0.4	0.2	0.1	0.3	0.3	20	18	25	21	81	66
P6	0.3	1.1	0.1	1.1	0.2	0.3	20	26	12	21	88	74
P7	0.9	0.7	0.3	0.3	0.6	0.4	35	30	42	21	107	91
P8	0.6	0.7	0.2	0.3	0.4	0.4	22	40	19	16	71	76
P9	0.6	0.3	0.2	0.1	0.4	0.2	30	20	31	28	119	105
P10	0.6	0.4	0.2	0.2	0.4	0.2	29	31	19	25	88	103
P11	0.4	0.2	0.2	0.1	0.2	0.1	20	30	15	29	98	92
P12	2.1	2.1	0.7	0.7	1.4	1.4	16	21	15	19	76	67
P13	1.2	1.2	0.6	0.7	0.3	1.2	28	26	25	32	83	66
P14	0.8	0.4	0.4	0.2	0.4	0.2	16	18	14	20	61	66
P15	0.9	1.2	0.3	0.4	0.6	0.8	15	23	29	33	92	79
P16	1.7	1.2	0.6	0.4	1.1	0.7	26	24	26	28	78	73
P17	0.7	0.5	0.3	0.2	0.4	0.3	19	19	29	20	107	97
P18	0.8	0.4	0.3	0.3	0.4	0.4	19	22	34	38	155	170
P19	0.9	0.7	0.3	0.2	0.6	0.5	21	24	27	36	76	59
P20	0.7	0.9	0.3	0.4	0.4	0.5	24	19	27	19	58	54

S. No.	Total Bilirubin		Direct Bilirubin		Indirect Bilirubin		SGOT (IU/L)		SGPT (IU/L)		Alkaline phosphatase	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P21	0.7	0.4	0.1	0.23	0.1	0.2	29	26	44	29.7	71	**55**
P22	0.2	0.55	0.14	0.22	0.2	0.3	14	15.4	14.5	10.7	84	70
P23	*0.36*	0.6	0.2	0.2	0.3	0.4	18	27	28	36	55	50
P24	*0.5*	0.5	0.3	0.2	0.5	0.3	38	23	25	22	92	55
P25	*0.8*	0.9	0.2	0.3	0.6	0.6	31	41	39	84	77	91
P26	*0.8*	0.7	0.4	0.3	0.4	0.4	16	16	14	18	46	31
P27	*0.8*	0.5	0.3	0.2	0.3	0.3	23	74	15	73	91	96
P28	*0.6*	0.3	0.2	0.1	0.4	0.2	20	17	14	25	65	53
P29	*0.6*	0.7	0.3	0.3	0.4	0.4	23	30	17	29	71	63
P30	*0.7*	0.9	0.33	0.4	0.5	0.5	25.7	51	42.2	92	76	68
P31	*0.8*	0.84	0.4	0.31	0.5	0.5	17	19.5	17	25	105	97
P32	*0.9*	1.1	0.4	0.4	0.5	0.7	17	24	17	25	105	72
P33	*0.9*	0.35	0.1	0.15	0.3	0.2	19	35.9	32	63.3	76	71
P34	*0.4*	0.5	0.22	0.2	0.3	0.3	22	24	16.7	18	60	53
P35	*0.51*	0.7	0.31	0.3	0.5	0.4	17.3	20	20.2	18	81	59
P36	*0.82*	1.2	0.6	0.5	0.8	0.7	51	16	46	11	118	74
P37	*1.4*	0.9	0.65	0.4	0.9	0.5	31.6	20	26.4	17	87	79
P38	*1.58*	0.6	0.3	0.2	0.4	0.4	16	22	26	36	89	71
P39	*0.7*	0.6	0.35	0.2	0.4	0.4	22.8	35	21.2	22	78	66
P40	*0.7*	1.1	0.8	0.4	1.6	0.7	19	21	29	22	97	80

S. No.	Blood (mg/dl)				Urea		Creatinine (mg/dl)		Urine Sugar (F)		Urine Sugar (PP)		Albumin		Deposits			
	Fasting (mg/dl)		Post Prandial (mg/dl)												Epi cells		Pus cells	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P1	82	90	121	86	19	6	0.7	0.7	Nil	Nil	Nil	Nil	Nil	Nil	Plenty of epi cells	1 to 2	Loaded pus cells	1 to 2
P2	80	83	91	99	12	14	1	1	Nil	Nil	Nil	Nil	Nil	Nil	3 to 5	1 to 2	4 to 6	1 to2
P3	108	104	168	179	14	25	1	1.1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P4	83	92	85	91	22	18	1	1.2	Nil	Nil	Nil	Nil	Nil	Nil	1 to 3	1 to 2	2to 4	1 to 2
P5	93	92	96	94	20	14	1.2	1.2	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 3	2 to 3	1 to 3
P6	94	96	115	88	17	13	0.9	0.9	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P7	99	93	139	105	14	10	1.1	1.1	Nil	Nil	Nil	Nil	Nil	Nil	2 TO 4	1 to 2	2 TO 4	1 to 2
P8	105	99	162	172	19	16	1	1	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	nil
P9	94	94	112	129	12	26	1	0.8	Nil	Nil	Nil	Nil	Nil	Nil	2 TO 4	2 TO 4	2 TO4	2 to 3
P10	88	86	93	99	15	14	0.9	0.9	Nil	Nil	Nil	Nil	4.3	Nil	2 to 4	1 to 2	2 to 4	1 to 2
P11	86	77	98	107	17	17	0.7	0.7	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	4 to 5	1 to 2
P12	102	76	120	115	15	20	0.9	0.9	Nil	Nil	Nil	Nil	Nil	Nil	1to 3	2 to 3	1 to 3	2 to 3
P13	96	89	127	117	23	20	1.1	1.1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P14	142	130	276	212	19	16	1	1	2+	2+	2+	2+	Nil	Nil	2 to 3	2 to 3	2 to 3	2 to 3
P15	128	122	235	264	16	29	0.9	0.9	2+	1+	2+	1+	Nil	Nil	1to 2	1 to 2	1 to 2	1 to2
P16	99	109	147	165	16	18	0.8	0.9	Nil	Nil	Nii	Nil	Nil	Nil	1 to 2	2 to 4	2 to3	2 to 3
P17	97	101	115	123	22	22	1	1	Nil	Nil	Nil	Nil	Nil	Nil	1to 2	1 to 2	1 to 2	2 to 3
P18	104	33	138	104	24	22	0.8	1	Nil	Nil	Nil	Nil	Nil	Nil	4 to 6	1 to 2	2 to 4	1 to 2
P19	101	94	123	134	18	22	0.9	0.9	Nil	Nil	Nil	Nil	Nil	Nil	1to 2	6-8	2 to 3	2 to 3
P20	99	82	144	234	16	20	1.2	1.2	1+	1+	1+	1+	Nil	Nil	1 to 2	2-3	1 to 2	2 to 3

S. No.	Blood (mg/dl)				Urea		Creatinine (mg/dl)		Urine Sugar (F)		Urine Sugar (PP)		Albumin		Deposits			
	Fasting (mg/dl)		Post Prandial (mg/dl)												Epi cells		Pus cells	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P21	77	89.8	133	89	24	23.3	1	1.1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P22	85.4	93.3	83	88	18.5	15.6	0.87	0.93	Nil	Nil	Nil	Nil	Nil	Nil	10 TO 12	2 TO 5	10 TO 12	2 TO 5
P23	101	99	114	119	22	19	1	1	Nil	Nil	Nil	Nil	Nil	Nil	2to4	2 to 3	4 to 6	2 to 4
P24	82	93	113	88	13	15	1.1	1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 3	1 to 2	1 to 3	1 to 2
P25	100	100	149	127	22	15	0.9	1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	2 to 4	2 to 4	1 to 2
P26	91	86	117	116	18	19	1.1	1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P27	88	90	124	127	19	29	0.8	0.8	Nil	Nil	Nil	Nil	Nil	Nil	1 to 3	2 to 4	2to 4	2to 4
P28	88	79	91	116	16	23	1.1	1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	2 to 4	1 to 2	1 to 2
P29	86	76	108	84	19	21	1.1	1	Nil	Nil	Nil	Nil	Nil	Nil	2 to 4	1 to 2	2 to 4	1 to 2
P30	89.2	91	115	124	18.3	16	1.11	1	Nil	Nil	Nil	Nil	4.3	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P31	96	73.1	128	85	27	15.4	0.8	0.85	Nil	Nil	Nil	Nil	Nil	Nil	2 to 4	1 to 2	1 to 2	2 to 3
P32	96	81	119	99	27	18	0.8	1.2	Nil	Nil	Nil	Nil	Nil	Nil	2 to 4	1 to 2	1 to 2	1 to 2
P33	86	79.6	95	125	16	17.1	1.1	1.09	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	2 to 3	1 to 2	2 to 4
P34	86.8	84	113	114	23.5	20	1.13	1.1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1 to 2	1 to 2	1 to 2
P35	75.7	77	125	96	17.7	16	1.03	1	Nil	Nil	Nil	Nil	Nil	Nil	2 to 3	2-3	2 to 3	1 to 2
P36	81	77	111	91	18	16	1	0.9	Nil	Nil	Nii	Nil	Nil	Nil	1 to 2	2-3	3 to 5	3 to 5
P37	77.5	76	82	93	17.4	24	1.09	1.1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	1-2	1 to 2	1 to 2
P38	85	73	98	103	22	18	1	1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	2-4	1 to 2	2 to 3
P39	82	71	164	130	21	20	0.94	0.9	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	6-8	1 to 2	1 to 2
P40	93	88	113	189	20	17	1	1	Nil	Nil	Nil	Nil	Nil	Nil	1 to 2	2-3	4 to 6	3 to 4

LIPIDPROFILE

S.NO	S. CHOL		HDL		LDL		VLDL		TGL	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P1	139	152	53	60	73	81	7	10	38	49
P2	223	215	48	49	95.8	121	34	31	173	156
P3	161	173	43	42	129	98	40	43	199	215
P4	197	195	55	50	109	90	21	20	107	105
P5	170	132	49	26	137	100	36	49	181	184
P6	145	161	41	47	78	87	35	23	175	114
P7	203	171	41	49	114	92	33	29	164	145
P8	182	143	55	44	87	78	26	30	132	150
P9	181	226	45	56	79	112	18	38	89	188
P10	199	179	58	49	92.8	87	14	14	72	68
P11	132	122	55	41	93	54	11	16	56	78
P12	114	113	41	31	95.6	53	22	33	110	164
P13	179	168	59	49	72	79	26	19	130	95
P14	119	125	40	38	88.5	52	15	12	77	106
P15	218	188	38	35	45.7	103	62	61	310	302
P16	239	217	45	44	69	118	50	35	250	176
P17	194	173	52	46	83.6	89	23	22	114	110
P18	162	154	37	35	107	77	20	21	98	110
P19	260	248	49	54	80.3	147	36	45	180	224
P20	177	175	47	45	97	98	18	27	89	137

S.NO	S. CHOL		HDL		LDL		VLDL		TGL	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P21	127	136	36	44	72	70.6	19	10.2	98	50.9
P22	*165*	169	47.6	56	133	89.3	20.2	15	*101.2*	75.1
P23	*219*	216	54	52	92	120	36	30	*179*	150
P24	*225*	250	57	54	110	143	29	44	*145*	219
P25	*217*	228	53	41	92	124	35	29	*176*	146
P26	*154*	132	85	55	82	56	16	15	*78*	75
P27	*206*	221	63	58	109	112	17	22	*88*	110
P28	*165*	154	45	39	108	72	37	30	*184*	435
P29	*153*	140	52	39	102	69	10	12	*53*	61
P30	*177*	158	54.3	40	108	77	18.7	16	*93.7*	77
P31	*185*	172	51	96.2	60	50.1	17	874	*84*	19.2
P32	*179*	135	33.9	33	57	70	45.7	25	*228.3*	124
P33	*143*	184	31	37.2	93	96.8	30	61.5	*148*	307.6
P34	*171*	166	33.9	36	64	92	26.6	33	*132.9*	163
P35	*194*	141	154.6	36	117	70	96.4	27	*30.9*	113
P36	*176*	145	84	38	118	74	12	20	*62*	100
P37	*192*	153	62.1	45	92	75	13.7	21	*68.6*	104
P38	*207*	175	44	40	80	97	29	23	*148*	119
P39	*177*	186	43.6	42	140	106	16.2	40	*80.9*	200
P40	*175*	199	42	46	91	113	28	41	*141*	206

S.NO	RA		ASO		CRP		VDRL		HBsAg	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P1	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P2	Negative	Negative	Negative	Negative	Positive	Positive	Non reactive	Non reactive	Negative	Negative
P3	Negative	Negative	Negative	Negative	Positive	Positive	Non reactive	Non reactive	Negative	Negative
P4	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P5	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P6	Positive	Positive	Positive	Positive	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P7	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P8	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P9	Negative	Negative	Negative	Negative	Positive	Negative	Non reactive	Non reactive	Negative	Negative
P10	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P11	Negative	Negative	Negative	Negative	Positive	Negative	Non reactive	Non reactive	Negative	Negative
P12	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P13	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P14	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P15	Negative	Negative	Negative	Negative	Positive	Negative	Non reactive	Non reactive	Negative	Negative
P16	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P17	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P18	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P19	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P20	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative

S.NO	RA		ASO		CRP		VDRL		HBsAg	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
P21	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P22	Negative	Negative	Negative	Negative	Positive	Positive	Non reactive	Non reactive	Negative	Negative
P23	Negative	Negative	Positive	Positive	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P24	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P25	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P26	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P27	Negative	Negative	Negative	Negative	Positive	Negative	Non reactive	Non reactive	Negative	Negative
P28	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P29	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P30	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P31	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P32	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P33	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P34	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P35	Negative	Negative	Positive	Positive	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P36	Negative	Negative	Positive	Positive	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P37	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P38	Negative	Negative	Negative	Negative	Negative	Negative	Non reactive	Non reactive	Negative	Negative
P39	Negative	Negative	Negative	Negative	Positive	Negative	Non reactive	Non reactive	Negative	Negative
P40	Negative	Negative	Positive	Positive	Positive	Negative	Non reactive	Non reactive	Negative	Negative

KALANJAGAPADAI (PSORIASIS)

CASE REPORT FORMS BOOK

Principal Investigator:

Dr.K.Archana,
PG scholar,
Department of SPM,
National Institute of Siddha,
Chennai-47.

Guide:

Dr.M.V.Mahadevan M.D(s),
Lecturer,
Department of SPM,
National Institute of Siddha,
Chennai-47.

From

Dr.K.Archana,

PG Scholar,

Department of Sirappu Maruthuvam,

National Institute of Siddha,

Chennai-47.

To

The Director,

National Institute of Siddha,

Chennai- 47.

Through Proper Channel

Respected Madam,

Sub: Submission of my Dissertation Protocol - regarding

I have selected "Pre clinical and comparative clinical trial of Siddha drugs ***Parangipattai Kudineer*** (Internally) and ***Sivappu Thylam*** (Externally) in the treatment of ***Kalanjagapadai*** (Psoriasis) with and without Yogam therapy (Agathavam Ettu)"as my dissertation work for the partial fulfillment of the requirement to degree of Doctor of Medicine in Sirappu Maruthuvam. I am herewith submitting my Protocol for your kind perusal and seek your permission to undertake my dissertation work.

Thanking you,

Place: Yours faithfully,

Date:

(Dr.K.Archana.)

PROTOCOL

"Pre clinical and comparative clinical trial of Siddha drugs ***Parangipattai Kudineer*** (Internally) and ***Sivappu Thylam*** (Externally) in the treatment of ***Kalanjagapadai*** (Psoriasis) with and without Yogam therapy (Agathavam Ettu)"

Principal Investigator:

Dr.K.Archana,

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Chennai-47.

Guide:

Dr.M.V.Mahadevan M.D(s),

Lecturer,

Department of Sirappu Maruthuvam,

National Institute of Siddha,

Chennai-47.

1.FULL TITLE OF STUDY:

"Pre clinical and comparative clinical trial of Siddha drugs ***Parangipattai Kudineer*** (Internally) and ***Sivappu Thylam*** (Externally) in the treatment of ***Kalanjagapadai*** (Psoriasis) with and without Yogam therapy (Agathavam Ettu)"

2.Name of the Candidate **:** Dr.K.Archana,

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3.Name of the Guide **:** Dr.M.V.Mahadevan M.D(s),

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Chennai-47.

4.BACKGROUND:

Siddha system of Medicine, one of the traditional system of practiced in India from time immortal known for its proven ability in curing long standing diseases and their life threatening complications. Siddhars have listed the diseases of mankind as 4448 based on the Mukkutram ie.,Vali, Azhal, Iyyam. Among them, the skin diseases are classified into 18 varieties by Siddhar Yugi Munivar. But he has not explained "Kalanjagapadai" as a separate entity. Instead of that he has described under the classification of vaadha diseases about "Kalanjagavatham" which may be correlated with Psoriatic arthropathy.

In the textbook "Siddha Maruthuvam Sirappu", Dr.R.Thiagarajan has described about Kalanjagapadai. The clinical features of Kalanjagapadai are correlated to psoriasis as described in modern dermatology.

In the Siddha system, skin disorders are brought under the clinical entity "Kuttam".

In the text book “Aathma Ratchamirtham ennum Vaiththiya saarasangiragam” the characteristics of kuttam are described as; white scaly patches will appear in foot, wrist and typical extensor distribution.

In the textbook “Siddha medical dictionary”, Mr.T.V.Sambasivam pillai has described

about “Kuttam” means cutaneous affections and so it is a comprehensive term used for various skin diseases. In this book “Sori kuttam” has been compared to psoriasis, a kind of leprosy with diffuse papular eruption with ulceration on the entire surface of the body marked by intense itching and burning sensation followed by exfoliation of the epidermis or browny scales (Eczematous psoriasis, lepra icthyosis).

Psoriasis is a common, chronic non infectious skin disease characterized by well defined slightly raised, dry erythematous macules with silvery scales and typical extensor distribution. (Ref: Practice of Dermatology- P.N.Bhel, Page no:253)

Psoriasis is a common chronic disfiguring inflammatory and proliferative epidermal skin disorder mediated by T cell that affect approximately 1 to 3% of the world population, multifactorial inheritance most likely a family history of psoriasis is found in 30% of patient.(Ref: Essential in Dermatology, pg. no: 82)

Psoriasis is universal in occurrence. There is a growing number of population-based studies providing worldwide prevalence estimates of psoriasis. Prevalence of psoriasis varies in different parts of the world. According to published reports, prevalence in different populations varies from 0% to 11.8%.Prevalence studies from India are mostly hospital-based. The prevalence of psoriasis to be 0.8% among the skin patients but the sample size of the study was very small. The ratio of male to female (2.46:1) was very high which could not be clearly accounted for. Highest incidence was noted in the age group of 20-39 years and the mean age of onset in males and females was comparable. (Ref:IJDVL-Indian Journal of Dermatology, Venerology and Leprologyhttp://www.ijdvl.com)

Some of the previous Dissertation study drugs for managing Psoriasis in National Institute of Siddha

S.No	INTERNAL MEDICINE	EXTERNAL MEDICINE	YEAR
1.	Chithiramoola Rasayanam	Veppannai Thylam	March2010
2.	Kirandimega Chooranam	Avuri Ennai	March2011
3.	Soolaikku perumarunthu chooranam	Viranangalukku Ennai	March2013
4.	Gandhaga Rasaayanam	Vettiver Thylam	March2014
5.	Karunchoorai chooranam	Kodiveli Thylam	March2015

The number of Kalanjagapadai patients attending the National Institute of Siddha hospital is increasing day by day. Patient is very much agitated and subjected to physical and mental suffering. However clinical symptoms can be relieved considerably with Siddha treatment.Siddhars identified numerous number of herbal for treating psoriasis. One such Siddha herbal formulation **"Parangipattai Kudineer" (Internal) and "Sivappu Thylam" (External)** mentioned in "Pharmacopoeia of hospital of Indian medicine" which is said to be cost effective, efficacious and simple formulation. This formulation has not undergone any clinical trial so far.

The ingredients of Parangipattai Kudineer are,

1.Parangipattai (Smilax china Linn.):

Anti-inflammatory,Anti-diabetic,Antispasmodic.

2.Kadugu Rohini (Picrorhiza kurroa Royle_):

Anti-inflammatory, Antioxident.

3.Manjitti (Rubia cordifolia Linn.):

Anti-inflammatory,Antianalgesic,Antipyretic.

4.Mara Manjal (Coscinium fenestratum Colebr.):

Antifungal, Antimicrobial, Anti-inflammatory, Antioxident,Antianalgesic.

5.Kadukkai (Terminalia chebula Retz.):

Antifungal, Antimicrobial, Anti-inflammatory, Antioxident.

6.Thandrikai (Terminalia bellarica Roxb.):

Antifungal, Antimicrobial, Anti-inflammatory.

7.Vasambu (Acorus calamus Linn):

Antifungal, Antimicrobial,Anti-inflammatory,Antianalgesic,Antipyretic,Antioxident.

8.Sombu (Pimpinella anisum Linn.) :

Anti-inflammatory,,Antianalgesic,Antifungal.

9.Veppampattai (Azadirachta indica A.Juss.):

Antifungal,Antimicrobial,Anti-inflammatory,Antianalgesic,Antipyretic,Antioxident.

10.Seendhil (Tinospora cordifolia Miers.):

Anti-inflammatory, Antianalgesic,Antipyretic,Anti-diabetic,Antispasmodic

The ingredients of Sivappu Thylam are,

1. Pungan Ver (Pongamia pinnata Pierre.):

Anti-inflammatory,,Antianalgesic,Antifungal,Antimicrobial

2. Manjitti (Rubia cordifolia Linn.:)

Anti-inflammatory,,Antianalgesic,Antipyretic.

3. Nannari (Hemides musindicus R.Br.) :

Antioxident,Anti-inflammatory

4. Manjal Mezhugu (Cera wax) :

Anti-inflammatory

5. Vellai Kungiliyam (Vateria indica Linn.):

Antispasmodic,Anti-inflammatory

6. Chevvallikkodi (Dioscoreapurpurea):

Anti-inflammatory

7. SurulPattai(Cinnamomumverum.Juss.):

Anti-inflammatory,,Antianalgesic

8. Coconut Oil (CocosnuciferaLinn.):

Anti-inflammatory,,Antianalgesic

So that I hope this medicine will be effective in the treatment of “KALANJAGAPADAI”. Therefore I have selected the drug for clinical study.

5.OBJECTIVES:

5.1.PRIMARY OBJECTIVE:

To evaluate the safety and therapeutic efficacy of Siddha drugs, *Parangipattai kudineer* (Internally) And *Sivappu Thylam*(Externally) in the treatment of *Kalanjagapadai* (Psoriasis)

5.2.SECONDARY OBJECTIVES

- To study the Siddha diagnostic methods such as *Envagai thervu* and *Manikkadai Nool* as complementary measures for diagnosis in Kalanjagapadai patients.
- To carry out the biochemical analysis of trail medicine *Parangipattai kudineer* (Internally)
- To evaluate the toxicity study of trail medicine *Parangipattai kudineer* (Internally)

6.JUSTIFICATION FOR THE CONDUCT OF THE STUDY:

Siddhars identified numerous number of herbal for treating psoriasis. One such Siddha herbal formulation **"Parangipattai Kudineer" (Internal) and "Sivappu Thylam" (External)** mentioned in "Pharmacopoeia of hospital of Indian medicine" which is said to be cost effective, efficacious and simple formulation. This formulation has not undergone any clinical trial so far.The ingredients of *Parangipattai kudineer* (Internally) are *Parangipattai (Smilax china.Linn.),Kadugu Rohini (Picrorhiza kurroa.Royle_), Manjitti (Rubia cordifolia.Linn.), Mara Manjal (Coscinium fenestratum.Colebr.), Kadukkai (Terminalia chebula Retz.), Thandrikai (Terminalia bellarica.Roxb.), Vasambu (Acorus calamus.Linn), Sombu (Pimpinella anisum.Linn.), Veppampattai (Azadirachta indicaA.Juss.),Seendhil (Tinospora cordifoliaMiers.)* are also having Antifungal, Antimicrobial, Anti-inflammatory, Antioxident, Antianalgesic. So that I hope this medicine will be effective in the treatment of KALANJAGAPADAI. Therefore I have selected the drug for clinical study.

7.METHODOLOGY:

7.1. STUDY TYPE : A preclinical and clinical study.

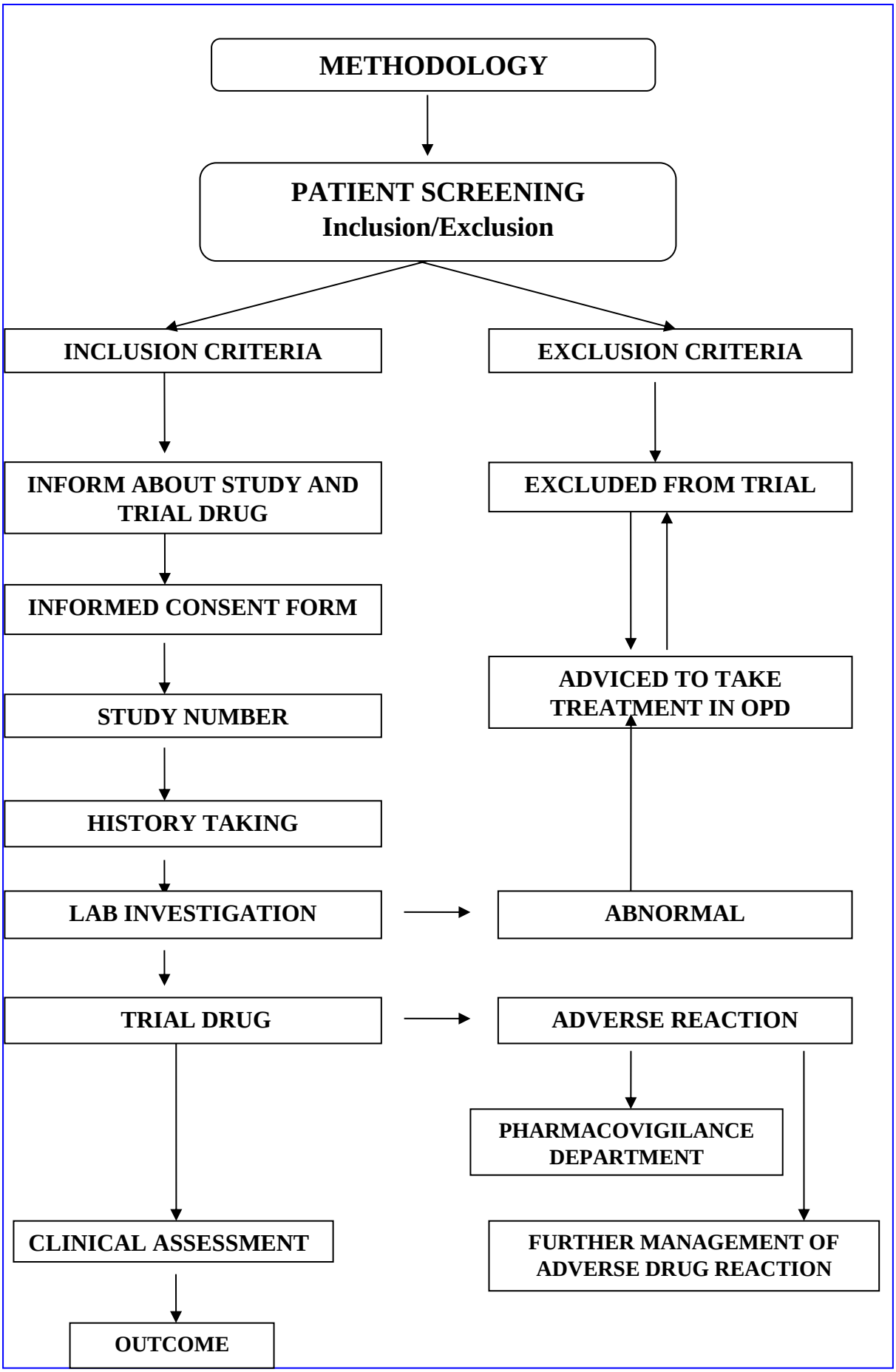
7.2. STUDY DESIGN:

Study Place : OPD and IPD of AyothidossPandithar Hospital,
National Institute of Siddha,
Tambaram Sanatorium, Chennai - 47.

Study Period : 18 Months

Year : 2016-2019.

Sample Size : 40 patients (20 Patients in OPD and 20 Patients in IPD)


METHODOLOGY
PATIENT SCREENING
Inclusion/Exclusion
INCLUSION CRITERIA
EXCLUSION CRITERIA
INFORM ABOUT STUDY AND TRIAL DRUG
EXCLUDED FROM TRIAL
INFORMED CONSENT FORM
ADVICED TO TAKE TREATMENT IN OPD
STUDY NUMBER
HISTORY TAKING
LAB INVESTIGATION
ABNORMAL
TRIAL DRUG
ADVERSE REACTION
PHARMACOVIGILANCE DEPARTMENT
CLINICAL ASSESSMENT
FURTHER MANAGEMENT OF ADVERSE DRUG REACTION
OUTCOME

7.3.DISEASE CONDITION:

Psoriasis is a common, chronic non infectious skin disease characterized by well defined slightly raised, dry erythematous macules with silvery scales and typical extensor distribution Kalanjagapadai correlated with Psoriasis.

The symptoms of Kalanjagapadai like red plaque,silvery white scales,on removal of scales minute bleeding point.

7.4 TRAIL DRUG :

Internal Medicine	**:** ***Parangipattai kudineer***
Dosage	**:** 30 ml , Three times a day (Before food)
Duration of Treatment	**:** 4 5 days
Reference	**:** Pharmacopoeia of hospital of Indian medicine
Page .No	**:** 3
Edition	**:** 2nd edition 1995
Edited & Publish by	**:** Directorate of Indian medicine & Homeopathy.
External Medicine	: **Sivappu Thylam**
Reference	**:** Pharmacopoeia of hospital of Indian medicine
Page.No	**:** 33
Edition	**:** 2nd edition 1995
Dosage	**:** Q.S. **(**Applied externally over the affected part**)**
Edited & Publish by	**:** Directorate of Indian medicine & Homeopathy.

Standard Operating Procedure:

Source of raw drugs:

The required raw drugs for the trial medicine will be purchased from a well reputed country raw drug shop and drugs will be authenticated by the competent authority Medicinal Botany and CCRS. After that the raw drugs will be purified separately then the trial drugs prepared in Gunapadam laboratory of National Institute of Siddha.

INTERNAL DRUG: ***PARANGIPATTAI KUDINEER***

Ingredients:

1.Parangipattai (Smilax chin. Linn.) ---1.000kg

2.KaduguRohini (Picrorhiza kurroa.Royle) ---1.000kg

3.Manjitti (Rubia cordifolia.Linn.) ---1.000kg

4.MaraManjal (Coscinium fenestratum.Colebr.)---1.000kg

5.Kadukkai (Terminalia chebula.Retz.) ---1.000kg

6.Thandrikai (Terminalia bellarica.Roxb) ---1.000kg

7.Vasambu (Acorus calamus.Linn.) ---1.000kg

8.Sombu (Pimpinella anisum.Linn) ---1.000kg

9.Veppampattai (Azadirachta indica.A.Juss) ---1.000kg

10.Seendhil (Tinospora cordifolia.Miers) ---1.000kg

METHOD OF PURIFICATION OF RAW DRUGS:

1. ***Parangipattai (Smilax china Linn.)***

It should be cleaned with white cloth then the outer layer of parangipattai root bark to be peeled out.(Ref: Sigicharathina theebam:28)

2. ***KaduguRohini (Picrorhiza kurroa.Royle.)***

It should be soaked in the neemleaf juice for 3 hours and it should be dried under sunlight.(Ref: Sigicharathina theebam:30)

3. ***Manjitti (Rubia cordifolia.Linn.)***

It should be dried under sunlight.(Ref: Sigicharathina theebam:30)

4. ***Mara Manjal (Coscinium fenestratum.Colebr)***

The outer skin should be removed.(Ref: Sigicharathina theebam:29)

5. ***Kadukkai(Terminalia chebula.Retz)***

The seed removed and rinds alone to be used for preparation.(Ref:Sigicharathina theebam:30)

6. ***Thandrikai (Terminalia bellarica.Roxb)***

The seed removed and rinds alone to be used for preparation.(Ref: Sigicharathina theebam:30)

7. ***Vasambu (Acorus calamus.Linn)***

It should be cleaned with white cloth then the outer layer of vasambu root bark to be peeled out (Ref: Sigicharathina theebam:30)

8. ***Sombu (Foeniculum vulgare.Linn)***

It should be dried for six hours under sunlight. (Ref: Sigicharathina theebam:29)

9. ***Veppam pattai (Azadirachta indica .A.Juss.)***

It should be cleaned with white cloth then the outer layer of veppampattai's bark to be peeled out.(Ref: Sigicharathina theebam:28)

10. ***Seendhil (Tinospora cordifolia .Miers.)***

The outer skin of stem should be removed. (Ref: Sigicharathina theebam:33).

METHOD OF PREPARATION:

All the drugs should be purified and crushed into coarse powder. Then adding 8 times of water with the coarse powder before boiling Preparing the decoction by reducing it into 1/8. Then filter and keep it for use.

7.5. Dosage : 30ml , Three times a day (Before food).

EXTERNAL MEDICINE: SIVAPPU THYLAM

Ingredients:

1. Pungan Ver (Pongamia pinnata Pierre.) -- 4kg

2. Manjitti (Rubia cordifolia Linn.) -- 62.5gm

3. Nannari (Hemidesmus indicus R.Br.) -- 62.5gm

4. Manjal Mezhugu (Cera wax) -- 62.5gm

5. Vellai Kungiliyam (Vateria indica Linn.) -- 62.5gm

6. Chevvallikkodi (Dioscorea purpurea) -- 20gm

7. Surul Pattai (Cinnamomum verum.Juss.) -- 30gm

8. Coconut Oil (Cocos nucifera Linn.) -- 1 Lr

METHOD OF PREPARATION :

Boil the Manjitti, Nannari, Chevvallikodi, PunganVer, adding 8 times of water. Prepare the decoction by reducing it into 1/8.Then equal quantity of oil should be mixed with the decoction and again to be boil.The yellow wax should be cut into pieces and added them into the melted thick consistency. After melting, it will be taken from the oven in the texture of sand. Then the pulverized Surulpattai (lavangapattai) added into it and stirr well.Then filter and keep it for use.

Drug Storage:

The trial drug ***Parangipattai Kudineer powder*** is stored in clean and dry container. ***Sivappu Thylam*** is stored in clean and dry narrow mouthed bottles.

Dispensing:

The *Parangipattai Kudineer powder 10gram/time* is given in packets and *Sivappu Thylam* quantity sufficient is given in bottles.

7.6.Duration : 45 days

7.7. Number of patients : 40 patients (20 Patients in OPD and 20 Patients in IPD)

Subject Selection:

Patients reporting with symptoms of Kalanjagapadai will be subjected to screening using screening Proforma. Then they will be allowed for the study fulfilling the following criteria:

7.8.Inclusion Criteria

- Age : 20-65 years
- Sex : Both male and female, Transgender
- History of Insulin Dependent Diabetes Mellitus
- Itching (with or without)
- Erythema
- Scaling
- Auspitz sign +
- Candle crease sign +
- Willing to give specimen of blood for the investigation whenever required.
- Willing to take photograph
- Willing to participate in trial and signing consent by fulfilling the condition of Proforma.

7.9.Exclusion Criteria

- History of Insulin Dependent Diabetes Mellitus
- Pregnancy and lactation
- History of Psoriasis with evidence of any other skin disease or Evidences of secondary infection in the lesions.
- History of Psoriatic arthropathy
- History of Cardiac diseases
- History of Hansen's disease
- History of any other chronic illness

Withdrawal Criteria

- Intolerance to the drug and development of any serious adverse effect during drug trial.
- Poor patient compliance & defaulters
- Patient unwilling to continue the course of clinical Study.
- Occurrence of any other systemic illness.

Tests and assessments:

1. Clinical assessment
2. Siddha system assessment
3. Routine investigations

1. **Clinical Assessment:**
   - Itching
   - Erythema
   - Macules
   - Papules
   - Pustules
   - Thickness
   - Scaling
   - Plaques
   - Hyper or hypopigmentation
   - Candle-grease sign
   - Auspitz sign
   - Koebner'sphenomenon

7.10. Investigations based on Siddha System:

I. ENVAGAI THERVU :

1. Naadi
2. Sparisam
3. Naa
4. Niram
5. Mozhi
6. Vizhi
7. Malam
8. Moothiram

- Neerkkuri :
- Neikkuri :

II. Manikadai Nool (Wrist circumetric sign): Finger breadths.

III. ELU UDAL THADHUKKAL:

1. Saaram :
2. Seneer :
3. Oon :
4. Koluppu :
5. Enbu :
6. Moolai :
7. Venneer or Suronidham :

2. INVESTIGATION:

Blood

- Hb
- Total WBC Count
- Polymorphs
- Lymphocytes
- Eosinophils
- Monocytes
- Basophils
- Total RBC count
- ESR : ½ Hr: 1 Hr:
- Blood sugar : Fasting: PP:
- Serum cholesterol

Urine

- Albumin
- Sugar (F) (PP)
- Deposits

Renal Function Tests

Blood Urea
Serum Creatinine
Uric acid

Liver Function Tests

Serum total bilirubin
Direct bilirubin
Indirect bilirubin
Serum Alkaline phosphatases
SGOT
SGPT

Skin Test :

- Candle-greasesign
- Auspitzsign
- Koebner'sphenomenon

9.Outcome:

- Good outcome - Clearance of lesions and Reduction of PASI Score from 3, 4 to 1,0
- Moderate outcome - Partial clearance of lesions and Reduction of PASI Score from 3, 4 to 2.
- Mild outcome - Slight clearance of lesions and Reduction of PASI Score from 4 to 3
- Nil outcome - No Clearance of lesions or No reduction PASI Score

Psoriasis Area and Severity Index (PASI)

A Psoriasis Area and Severity Index (PASI) is a quantitative rating scale for measuring the severity of psoriatic lesions based on area coverage and plaque appearance

Erythema / Thickness / Scaling-Rating score	**Area Scoring**
0 - None	0-Nil
1- Slight	1-1-9%
2- Moderate	2- 10%-29%
3-Severe	3-30%-49%
4-Very severe	4-50%-69%
	5-70%-89%
	6-90%-100%

PASI CALCULATION

Plaque Characteristic	Rating Score	Body region and weighting factor			
		Head	Upper Limbs	Trunk	Lower Limbs
Erythema	0 = None				
Thickness	1 = Slight				
	2 = Moderate				
Scaling	3 = Severe				
	4 = Very Severe				
Totals					
Weighting Factor		x 0.1	x 0.2	x 0.3	x 0.4
Surface area totals					
Degree of involvement as % for each body region affected (score each region between 0 and 6)	0 = None				
	1 = 1-9%				
	2 = 10-29%				
	3 = 30-49%				
	4 = 50-69%				
	5 = 70-89%				
	6 = 90-100%				
Surface area totals x % involvement totals Sum Scores above =					

- **Add together each of <u>Erythema/Thickness/Scaling</u> scores for each of the body regions to give 4 separate sub totals A1, A2, A3 and A4**
- **Multiply each sub total by amount of body surface area represented by that region i.e. A1 x 0.1 for head, A2 x 0.2 for upper limbs, A3 x 0.3 for trunk, A4 x 0.4 for lower limbs to give a value B1, B2, B3 and B4 for each body region respectively.A1 x 0.1=B1; A2 x 0.2=B2; A3 x0.3=B3; A4 x 0.4=B4**
- **For each body region multiply sub total B1, B2, B3 and B4 by the score(0-6) of the % of body region involved to give 4 sub totals C1, C2, C3 and C4**
- **The patient's PASI score is the sum of C1+C2+C3+C4**

10. Conduct of the study:

Group I : Trail drug without yogam in OPD patients.

Group II : Trail drug with yogam in IPD patients.

First day :

Agathiyar kulambu with 200mg with 30ml leaf juice of Sangankuppi (*Azima tetracantha*) quantity was administered at early morning as purgative (*Kazhichal* Medicine) before starting the treatment for restore equilibrium of dhoshams.

Second day :

Oil bath with *Arakku thylam* has taken at early morningfor restore equilibrium of udalthathus.

Third day onwards from Sunday,Tuesday,Thursday for 48 days :

Internal Medicine: *Parangipattai Kudineer*, three times a day before food.

External Medicine: *Sivappu thylam*

Advice for method of topical therapy :

Oil applied in psoriatic lesion by cotton for 4 hrs at 1pm to 5pm and take sunbath at 4pm to 5.30pm thereafter bath with warmwater used by greengram powder.

Yogam therapy (Agathavam Ettu) will be given for IPD patients. Envagai Thervu will be evaluvate before and after the treatment for 40 patients. Nei Kuri will be evaluvate 0^{th}day,15^{th} day,49^{th} dayof the treatment for opd and IPD patients. Manikadai Nool will be measure before the treatment for 40 patients.

OPD patients are requested to visit the hospital once in 7 days. In each and every visit clinical assessment and prognosis were recorded. For IPD patients the clinical assessment and prognosis were recorded daily.

Laboratory investigations were done before and after the trial. For IPD patients, who are not in a position to stay in the hospital for a long time are advised to attend the OPD for further follow-up. At the end of the trial, the patients are advised to visit the OPD.

CLINICAL APPLICATION OF MANIKADAI NOOL TECHNIQUE :

Manikadai nool is one among the tool of examination in siddha system to diagnose the disease as well as to assess its prognosis. This unique method was revealed by siddhar AGATHIYR to his disciple Vedhamamuni.The literary meaning of the terminology ;

PROCEDURE ;

The circumference of the forearm of an individual at the region of 4 finger breadth proximal to the radial protuberance of wrist is measured by using a thread, which should be non elastic. Then the length of the thread is converted in terms of finger breadth units (viral kadai) of the concerned individual patient.

11.Ethical issues:

- The internal drug was mentioned in the List of books of Drugs and Cosmetics Act 1940. Hence no preclinical and toxicity studies will be carried out.
- The patient will be informed about the treatment and other procedures in his vernacular language. After getting the consent only (language understandable to the patient) they will be enrolled in the study.
- To prevent any infection, while collecting blood sample from the patient, only disposable syringes, disposable gloves, with proper sterilization of lab equipments will be used.
- The data collected from the patient will be kept confidential.
- Treatment will be provided free of cost.
- If any adverse reactions occur it will be reported to the Pharmacovigilance committee of NIS. And they will be advised to take treatment at the OPD of National Institute of Siddha.

12.Data collection:

Required information will be collected from each patient by using the following forms:

Forms:

Form I	Screening and selection Proforma
Form II	History taking &Clinical assessment Proforma
Form III	Laboratory investigation Proforma
Form IV	Drug compliance form

Form V	Patient information sheet
Form VI	Consent form
Form VII	Withdrawal form
Form VIII	Dietary Advice form

Study Enrolment:

- Patients reporting at the OPD with clinical feature of erythematous patches, silvery scaling are chosen for enrolment based on the inclusion and exclusion criteria.
- The enrolled patients will be informed about the study, trial drug, possible outcomes and the objectives of the study in the language and terms understandable to them and getting consent in the Informed Consent form (Form VI).
- Complete clinical history, complaints and duration, examination findings-- all would be recorded in the prescribed Proformas.
- Screening Form- I will be filled up, Form –II and Form –III will be used for recording the patients, history, clinical examination of symptoms and signs and laboratory investigations respectively. If there is any abnormal laboratory reports obtained then excluded from this study. Patients would be advised to take the trial drug and appropriate dietary advice (Form VIII) would be given according to the patients, perfect understanding.

13.Pharmaco-Vigilance (Adverse/serious adverse effects management):

If the trial patient develops any adverse reaction, he/she would be immediately withdrawn from the trial and he will be directed to take treatment in OPD of NIS. It will also be reported to the Pharmaco-vigilance committee of NIS.

14.Dermatology Life Quality Index (DLQI):

Recent studies have emphasized the association of psoriasis severity with impaired physical and public functioning as well as with the emotional state. The DLQI is calculated by summing the score of each question resulting in a minimum of 0 and a maximum of 30. The higher the score, the more quality of life is impaired.

15.Outcome measures:

The outcome of the study was clinically observed by the PASI Score.

PASI Score: -

*** PASI 25** = 25% **(Poor)** reduction in the PASI Score in before and after treatment.

*** PASI 50 =** 50% **(Moderate)** reduction in the PASI Score in before and after treatment.

*** PASI 75 =** 75% **(Good)** reduction in the PASI Score in before and after treatment.

16.Data analysis:

After enrolling the patients in the study, a separate file for each patient will be maintained and all forms will be kept in the file. Study No. and patient's No. will be entered on the top of the file for easy identification. Whenever the patients visit OPD during the study period, necessary entries will be made at the assessment forms.

The screening forms will be filled separately. All forms will be further scrutinized by Senior Research Officer (Statistics) for logical errors and incompleteness of data to avoid any bias. No modification in the results is permitted for unbiased reports

References:

- *Pharmacopoeia of hospital of Indian medicine, Page No :3 and 33*
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- *Siddha MateriaMedica (Medicinal Plants Division) – Vaithiya Rathinam.K.S.Murugesa mudhaliyar.*
- *Aathma Ratchamirtham ennum Vaiththiya saarasangiragam –Mr.Kandhasami mudhaliyar.*
- *Siddha medical dictionary – Mr.T.V.Sambasivam pillai.*
- *Sigicha rathina theebam – Mr.C.Kannusami pillai.*
- *Agathiyar Soodamani Kayaru Soothiram.*

NATIONAL INSTITUTE OF SIDDHA
AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF SIRAPPU MARUTHUVAM

PRE CLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM (***EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU).

Principal Investigator: Dr.K.ARCHANA **CTRI REG.NO : CTRI/2018/07/015115**

FORM - SCREENING & SELECTION PROFORMA

1.SERIAL NO: **2. OP /IP NO:**
3. NAME: **4. AGE/GENDER:**
5. OCCUPATION: **6. INCOME:**

INCLUSION CRITERIA

- Age : 20-60 years YES\ NO
- Sex : Male,Female and Transgender M \ F\T
- History of Non-Insulin Dependent Diabetes Mellitus YES\ NO
- Erythema YES\ NO
- Thickness YES\ NO
- Scaling YES\ NO
- Itching :with or without itching YES\ NO
- Auspitz sign + YES\ NO
- Candle crease sign + YES\ NO
- Willing to attend OPD or admission in IPD for the trial YES\ NO
- Willing to give specimen of blood for the investigation YES\ NO
- Willingness for consent YES\ NO
- Willing to take photograph before and after treatment. YES\ NO

EXCLUSION CRITERIA

- History of Insulin Dependent Diabetes Mellitus YES\ NO
- Pregnancy and lactation YES\ NO
- Psoriasis with evidence of any other skin disease YES\ NO
- Psoriatic arthropathy YES\ NO
- Cardiac disease YES\ NO
- Hansen's disease YES\ NO
- Evidences of secondary infection in the lesions YES\ NO
- Any other chronic illness YES\ NO

ADMITTED TO TRAIL

YES ☐ NO ☐
If Yes, OPD ☐ IPD ☐
Serial NO: ☐

Date:
Station:
Signature of the Investigator:
Signature of the Lecturer: **Signature of the HOD:**

NATIONAL INSTITUTE OF SIDDHA
AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF SIRAPPU MARUTHUVAM

PRE CLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM (***EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU).

FORM- INFORMATION SHEET

Name of Principal Investigator **:** Dr.K.ARCHANA
CTRI REG.NO **: CTRI/2018/07/015115**

Name of the institute **:** National Institute of Siddha,
Tambaram Sanatorium,
Chennai-47.

INFORMATION SHEET FOR PATIENTS PARTICIPATING IN THE OPEN CLINICAL TRIAL:

I, Dr.K.Archana Studying as M.D (Siddha) at National Institute of Siddha, Tambaram Sanatorium is doing a trial on the study *Kalanjagapadai* (Psoriasis). Psoriasis is a most common persistent skin disease, occurring throughout the world. The symptoms of *Kalanjagapadai* like red plaque, silvery white scales, on removal of scales minute bleeding point. This condition is being treated in NIS with many siddha formulations. As a part of M.D(S) research programme and developing new efficacious medicine, I propose to study the *Parangipattai Kudineer* formulation for treating the *Kalanjagapadai.* This formulation has been mentioned in siddha literature and empirical evidence with contemporary tools is required for documentation. You can the receive medicines free of cost *Parangipattai Kudineer* powder (Internal medicine) 10g three times a day Sivappu Thylam (External medicine), for 7 days in a duration of 45 days without any cost. You have to visit OPD 7 days once (7 visits) during the 45 days and if you wish to stay in the In Patient ward and Yogam therapy (Agathavam Ettu)- Surya namaskaram (Sun salutation), Padmasanam (Lotus position),Nadi suddhi pranayamam (Alternate nostril breathing practice), Paschimottanasanam (Forward bend pose), Makarasanam (Crocodile pose) will be given for IPD patients. I will assess the effect of treatment after completion of 45 days of treatment using clinical and lab parameters.

- At each visit, the study physician (investigator) will be examine you. Blood tests will be carried out before study initiation and after the study completed. Blood will be collected at that time .Blood collection involves prick with a sterile needle and syringe.

 In this regard, I need to ask you few questions. I will maintain confidentiality of your comments and data obtained from you. There will be no risk of disclosing your identity and no physical, psychological or professional risk is involved by taking part in this study.

Taking part in this study is voluntary. No compensation will be paid to you for taking part in this study. You can choose not to answer any specific question. In this study, you will get treatment benefits and free investigations. Taking part in the study may be of benefit to the community, as it may help us to develop medicine for *Kalanjagapadai* . In case of any adverse symptoms which is expected for few patients during the treatment, please report to me and care will be taken in OPD of NIS. You can withdraw from the study at the midst of treatment period, if you are not interested to continue and you will receive our usual treatment without condition. If you agree to be a participant in this study, you will be screened as per the study protocol.

 If you wish to find out more about this study before taking part, you can ask me all the questions by contact Dr.K.Archana PG scholar cum principal investigator of this study, attached to the National Institute of Siddha, Chennai (Mobile phone no:8675544027). You can also contact the Chairman/Member-secretary of Ethics committee, National Institute of Siddha, Chennai – 600045, Tel no: 91-44-22411611, for rights and participation in the study.

தேசிய சித்த மருத்துவ நிறுவனம், சென்னை 47

அயோத்திதாசர் பண்டிதர் மருத்துவமனை

FORM - தகவல் படிவம்

***காளாஞ்சகப்படை* நோய்க்கான சித்த மருந்து *பறங்கிப்பட்டைக் குடிநீர்* (உள்மருந்து) *சிவப்புத் தைலம்* (வெளி மருந்து) பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்விற்கான தகவல் படிவம்.**

முதன்மை ஆராய்ச்சியாளர் பெயர் : மரு. க.அர்ச்சனா

CTRI REG.NO : CTRI/2018/07/015115

நிறுவனத்தின் பெயர் : தேசிய சித்த மருத்துவ நிறுவனம்
தாம்பரம் சானட்டோரியம்
சென்னை 47

மரு.க.அர்ச்சனா ஆகிய நான் தேசிய சித்த மருத்துவமனையில் பட்ட மேற்படிப்பு பயின்று வருகிறேன். *காளாஞ்சகப்படை* என்னும் நோயானது சித்த மருத்துவத்தில் தோலைப் பாதிக்கும் ஒரு நோயாகும். இந்த நோயில் தோலில் சிவப்பு நிறத் திட்டுகளை ஏற்படுத்தி அதில் செதில் போல் உதிர செய்யும் சில சமயம் அரிப்புடனோ அல்லது அரிப்பின்றியோ காணப்படும். - து மற்றவர்களுக்கு பரவ கூடிய நோய் அல்ல. இந்நோய்க்கு தேசிய சித்த மருத்துவமனையில் பல சித்த மருந்துகள் பயன்படுத்தப்பட்டு வருகின்றது. சித்த மருத்துவ பட்ட மேற்படிப்பில், ஆய்வின் ஒரு பகுதியாக புதிய மருந்துகளை பயன்படுத்தும் நோக்கில் *பறங்கிப்பட்டைக் குடிநீர் (உள்மருந்து) சிவப்புத் தைலம் (வெளி மருந்து)* மருந்தினை இந்நோய்க்கு வழங்க பரிந்துரை செய்கிறோம். இந்த மருந்தின் செய்முறை, அளவு, மற்றும் மருத்துவ பயன்கள் அனைத்தும் அங்கீகரிக்கப்பட்ட சித்த மருத்துவ நூலில் கூறப்பட்டுள்ளது. எந்தவித கட்டணமுமின்றி தாங்கள் இந்த மருந்தினை பெற்றுக்கொள்ளலாம். இந்த ஆய்வில் மருந்து உட்கொள்ளும் காலம் 45 நாட்கள் ஆகும். 7 நாட்களுக்கு ஒருமுறை தேசிய சித்த மருத்துவமனைக்கு நேரில் வந்து 7 நாட்களுக்கான மருந்தினை பெற்றுக்கொள்ள வேண்டும். உள்நோயாளர்களுக்கு *யோக மருத்துவம் (அகத்தவம் எட்டு) - சூரிய நமஸ்காரம், பத்மாசனம், நாடிசுத்தி பிராணயாமம், பட்சிமோத்தாசனம், மகராசனம்* தினமும் பரிந்துரை செய்யப்படும். இந்த ஆய்வு சம்பந்தமான ஆய்வக பரிசோதனைகள் கட்டணமின்றி செய்யப்படும்.45 நாட்கள் மருந்து உட்கொள்ளும் காலம் முடிந்த பிறகு நோய்க்கான குறிகுணங்கள் மற்றும் ஆய்வக பரிசோதனைகள் இவற்றின் முடிவுகளின் அடிப்படையில் மருந்தின் பரிகரிப்புத்திறன் கண்டறியப்படும்.

இந்த ஆய்வு சம்பந்தமாக சில கேள்விகளை தங்களிடம் கேட்க இருக்கிறேன். தங்களிடமிருந்து பெறப்படும் கருத்துக்கள் மற்றும் குறிப்புகள் அனைத்தும் நம்பிக்கையாக

பதிவு செய்யப்படும். இந்த ஆய்வில் தங்களை உட்படுத்திக்கொள்வதின் மூலம் எந்த வகையிலும் பாதிப்புக்குள்ளாக மாட்டீர்கள் என உறுதி அளிக்கிறேன்.

எந்தவித வற்புறுத்தலுமின்றி, இந்த ஆய்வில் பங்கேற்கவும், இந்த ஆய்வு சம்பந்தமாக கேட்கப்படும் கேள்விகளுக்கு பதில் கூறவும் தங்களுக்கு முழு சுதந்திரம் அளிக்கப்படுகிறது. கேள்வி பதில் வடிவத்தில் தங்களிடம் கேள்விகள் கேட்கப்படும்.இந்த ஆய்வில் பங்கேற்பதற்கு எந்த சன்மானமும் வழங்கப்படமாட்டாது. ஆனால், ஆய்வு முழுவதும் எனது மேற்பார்வையிலும், தங்கள் உடல்நலன் குறித்த தனி கவனத்திலும் ஆய்வு மேற்கொள்ளப்படும். *காளாஞ்சகப்படை* நோய்க்கான புதிய மருந்தின் பரிகரிப்புத்திறனை சமூகத்திற்கு உணர்த்தும் வகையில் இந்த ஆய்வு மேற்கொள்ளப்படுகிறது.இந்த ஆய்வின் போது உடலுக்கு வேறு பாதிப்பு ஏற்படும் பட்சத்தில் இம்மருத்துவமனையில் தக்க மாற்றுசிகிச்சை அளிக்கபடும். இந்த ஆய்வினைத்தொடர தங்களுக்கு விருப்பம் இல்லையெனில், எப்பொழுது வேண்டுமானலும் ஆய்வின் இடையில் விலகிக்கொள்ளவும், இம்மருத்துவமனையில் வழங்கப்படும் இந்நோய்க்கான வழக்கமான மருந்துகளை பெற்றுக்கொள்ளவும் அறிவுறுத்தப்படுகிறீர்கள்.

இந்த ஆய்வில் சேகரிக்கப்படும் விபரங்கள் அனைத்தும் தங்களுக்கும் முதன்மை ஆராய்ச்சியாளரான எனக்கும் இடையில் இரகசியமாக வைக்கப்படும்..நீங்கள் இந்த ஆய்வில் பங்கேற்க விருப்பப்பட்டால், திட்ட வரைவு படி தேர்வு செய்யப்படுவீர்கள்.

நீங்கள் இந்த ஆய்வில் பங்கேற்கும் முன், இந்த ஆய்வினைப் பற்றிய மேலும் விபரங்கள் பெற வேண்டுமென விருப்பப்பட்டால், இந்த ஆய்வின் முதன்மை ஆராய்ச்சியாளர் மற்றும் தேசிய சித்த மருத்துவமனை, பட்ட மேற்படிப்புத்துறை மாணவி மரு. க.அர்ச்சனா ஆகிய எண்ணை 8675544027 என்ற எண்ணில் தொடர்பு கொள்ளலாம். மேலும், நீங்கள் இந்த ஆய்வில், உங்களது பங்கேற்பு மற்றும் உரிமை பற்றி தெரிந்து கொள்ள தேசிய சித்த மருத்துவமனை, தலைவர்/செயற்க்குழு உறுப்பினர் அவர்களையும் 91-44-22711611 என்ற எண்ணில் தொடர்பு கொள்ளலாம்.

NATIONAL INSTITUTE OF SIDDHA
AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF SIRAPPU MARUTHUVAM

PRE CLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM (***EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU).

Principal Investigator: Dr.K.ARCHANA
CTRI REG.NO : CTRI/2018/07/015115

FORM – CONSENT FORM

*"**I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction.***

***I consent voluntarily to participate as a participant in this study and understand that I have the right to withdraw from the study at any time without in any way it affecting my further medical care**".*

"I have received a copy of the information sheet/consent form".

Date:

Signature of the participant

In case of illiterate participant

*"**I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm individual has given consent freely**."*

Date:

Signature of a witness
(Selected by the participant bearing no connection with the survey team)

Left thumb Impression of the Participant

தேசிய சித்த மருத்துவ நிறுவனம், சென்னை 47

அயோத்திதாசர் பண்டிதர் மருத்துவமனை

FORM – ஒப்புதல் படிவம்

காளாஞ்சகப்படை நோய்க்கான சித்த மருந்து பறங்கிப்பட்டைக் குடிநீர் (உள் மருந்து) சிவப்புத் தைலம் (வெளி மருந்து) பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்விற்கான ஒப்புதல் படிவம்.

முதன்மை ஆராய்ச்சியாளர் பெயர் : மரு.க.அர்ச்சனா.**CTRI REG.NO : CTRI/2018/07/015115**

நிறுவனத்தின் பெயர் : தேசிய சித்த மருத்துவ நிறுவனம்

தாம்பரம் சானட்டோரியம்

சென்னை 47

ஆய்வாளரால் சான்றளிக்கப்பட்டது :

நான் காளாஞ்சகப்படை என்னும் நோயின் ஆய்வைக் குறித்த அனைத்து விபரங்களையும் நோயாளிக்குப் புரியும் வகையில் எடுத்துரைத்தேன் என உறுதியளிக்கிறேன்.

தேதி: **கையொப்பம்:**

இடம்: **பெயர்:**

நோயாளியின் ஒப்புதல்

என்னிடம் இந்த மருத்துவ ஆய்வின் காரணத்தையும், மருந்தின் தன்மை மற்றும் மருத்துவ வழிமுறை பற்றியும், தொடர்ந்து எனது உடல் இயக்கத்தைக் கண்காணிக்கவும், அதனைப் பாதுகாக்கவும் பயன்படும் மருத்துவ ஆய்வுக்கூட பரிசோதனைகள் பற்றி திருப்தி அளிக்கும் வகையில் ஆய்வு மருத்துவரால் விளக்கிக் கூறப்பட்டது. நான் இந்த மருத்துவ ஆய்வின் போது, எப்பொழுது வேண்டுமானாலும் இந்த ஆய்விலிருந்து என்னை விடுவித்து கொள்ளும் உரிமையைத் தெரிந்திருக்கின்றேன்.

நான் என்னுடைய சுதந்திரமாகத் தேர்வு செய்யும் உரிமையைக் கொண்டு காளாஞ்சகப்படை நோய்க்கான ***பறங்கிப்பட்டைக் குடிநீர் (உள்மருந்து) சிவப்புத் தைலம் (வெளி மருந்து)*** மருந்தினை பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்விற்கு என்னை உட்படுத்த ஒப்புதல் அளிக்கிறேன்.

சாட்சிக்காரர் :1.கையொப்பம்:

தேதி: **பெயர்:**

இடம்: **உறவுமுறை:**

2.கையொப்பம்:

பெயர்:

உறவுமுறை:

விரிவுரையாளார் கையொப்பம்: **துறைத்தலைவர் கையொப்பம்:**

NATIONAL INSTITUTE OF SIDDHA
AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF SIRAPPU MARUTHUVAM

PRECLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM (***EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU).

Principal Investigator: Dr.K.ARCHANA

CTRI REG.NO : CTRI/2018/07/015115

FORM : HISTORY TAKING PROFORMA

STUDY NO: **OP / IP NO:**
NAME: **AGE / GENDER:**
ADDRESS: **CONTACT NO :**
RELIGION : H / C / M / O.
OCCUPATION: **INCOME:**
MARITAL STATUS : 1. Married 2. Unmarried
DATE OF INTIAL ASSESSMENT:

COMPLAINTS & DURATION: (BEFORE TREATMENT)	**COMPLAINTS & DURATION: (AFTER TREATMENT)**

PERSONAL HISTORY:

PERSONAL HABITS	**YES**	**NO**	**IF YES SPECIFY DURATION**	**AMOUNT/Qty**
Smoking				
Betel leaf , Tobacco Chewing				
Alcohol				
Narcotic Drug Addiction				

HISTORY OF PREVIOUS ILLNESS AND TREATMENT TAKEN:

FAMILY HISTORY:
Whether this problem runs in family? 1. Yes 2. No

If yes, mention the relationship of affected person(s)

1._____

2._____

DIETARY STYLE: 1. Vegetarian 2. Non-vegetarian

MENSTURAL AND OBSTETRIC HISTORY:

ANY ALLERGY HISTORY :

FORM II B

GENERAL EXAMINATION:	**Before treatment**	**After treatment**
1. Conscious / Oriented /Co-operative / Comfortable / Unconscious /Comatose :		
2. Body weight [Kg] :		
3. Height [cms] :		
4. BMI :		
5. Body Temperature [F] :		
6. Blood Pressure (mm/Hg) :		
7. Pulse Rate /min. :		
8. Heart Rate / min. :		
9. Respiratory Rate /min. :		
10. Facies :		
11. Head and neck :		
12. Mouth and oral cavity :		
13. Skin and Hair :		
14. Extremities :		
15. Joints :		
16. Genitalia :		
17. Hernial orifices :		
18. Abdominal distension :		
19. Pallor :		
20. Icterus :		
21. Clubbing :		
22. Cyanosis :		
23. Pedal Oedema :		
24. Lymphadenopathy :		
25. Jugular venous pulsation :		

SYSTEMIC EXAMINATION	**: Before treatment**	**After treatment**
Cardiovascular system	**:**	
Respiratory system	**:**	
Gastro-intestinal system	**:**	
Central Nervous system	**:**	
Urogenital system	**:**	
Endocrine system	**:**	

SIDDHA SYSTEM OF EXAMINATION

1. THEGI (BODY CONSTITUTION):

1. Vathaudal ☐
2. Pithaudal ☐
3. Kabaudal ☐
4. Thonthaudal ☐

2. NILAM (LAND WHERE THE PATIENT LIVED MOST):

1. Kurinji(Hilly terrain) ☐
2. Mullai (Forest range) ☐
3. Marutham (Plains) ☐
4. Neithal (Coastal belt) ☐
5. Paalai (Aridregion) ☐

3. KAALAM: **Before treatment** **After treatment**

1. Kaarkaalam (Aavani-Purattasi)
2. Koothirkaalam (Ippasi-Kaarthigai)
3. Munpanikaalam (Maargazhi-Thai)
4. Pinpanikaalam (Maasi-Panguni)
5. Ilavenilkaalam (Chithirai-Vaigasi)
6. Muthuvenilkaalam (Aani-Aadi)

4. GUNAM:

1. Sathuvam ☐
2. Rasatham ☐
3. Thamasam ☐

5. PORIPULANGAL (SENSORY ORGANS):

	Before treatment	**After treatment**
Mei (Skin)	Normal / Affected	Normal / Affected
Vai (Tongue)	Normal / Affected	Normal / Affected
Kann (Eye)	Normal / Affected	Normal / Affected
Mooku (Nose)	Normal / Affected	Normal / Affected
Sevi (Ear)	Normal / Affected	Normal / Affected

6.KANMENDRIYAM (MOTOR ORGANS) :

	Before treatment	**After treatment**
Kai(Upper limb)	Normal /Affected	Normal /Affected
Kaal(Lower limb)	Normal /Affected	Normal /Affected
Vai (Oral cavity)	Normal /Affected	Normal /Affected
Eruvai(Anal region)	Normal /Affected	Normal /Affected
Karuvai(Uro-Genital region)	Normal /Affected	Normal /Affected

7.KOSANGAL (SHEATH):

	Before treatment	**After treatment**
Annamayakosam	Normal /Affected	Normal /Affected
Pranamayakosam	Normal /Affected	Normal /Affected
Manomayakosam	Normal /Affected	Normal /Affected
Vignanamayakosam	Normal /Affected	Normal /Affected
Ananthamayakosam	Normal /Affected	Normal /Affected

8. SEVEN UDAL THAATHUKKAL (SEVEN SOMATIC COMPONENTS)

	Before treatment	**After treatment**
Saaram	Normal /Affected	Normal /Affected
Senneer	Normal /Affected	Normal /Affected
Oon	Normal /Affected	Normal /Affected
Kozhuppu	Normal /Affected	Normal /Affected
Enbu	Normal /Affected	Normal /Affected
Moolai	Normal /Affected	Normal /Affected
Sukkilam / Suronitham	Normal /Affected	Normal /Affected

9. UYIR THAATHUKKAL: [THREE HUMORS] (VALI/ AZHAL/ IYYAM)

A) VAL

	1st day	8th day	15th day	22nd day	29th day	36th day	41th day	48th day
Praanan								
Abaanan								
Samaanan								
Udhaanan								
Viyaanan								
Naagan								
Koorman								
Kirukaran								
Devathathan								
Dhananjeyan								

B) AZHAL

	1st day	8th day	15th day	22nd day	29th day	36th day	41th day	48th day
Analakam								
Ranjakam								
Saathakam								
Prasakam								
Aalosakam								

C) IYYAM

	1st day	8th day	15th day	22nd day	29th day	36th day	41th day	48th day
Avalambagam								
Kilethagam								
Pothagam								
Tharpagam								
Santhigam								

10. ENVAGAI THERVU: [EIGHT TYPES OF EXAMINATION]

I. NAADI: [PULSE PERCEPTION]

NAADI	1st day	8th day	15th day	22nd day	29th day	36th day	41th day	48th day

II. SPARISAM: [PALPATION]

Day	SPARISAM
1st day	
8th day	
15th day	
22nd day	
29th day	
36th day	
41th day	
48th day	

III. NAA: [TONGUE]

NAA	1st day	8thday	15thday	22nddday	29thday	36thday	41thday	48th day

IV.NIRAM: [COMPLEXION] : BEFORE TREATMENT :AFTER TREATMENT

V.MOZHI: [VOICE]

1. High Pitched ☐
2. Low Pitched ☐
3. Medium Pitched ☐

VI.VIZHI: [EYES]

VIZHI	1st day	8th day	15thday	22nddday	29thday	36th day	41thday	48thday

VII. MALAM: [BOWEL HABITS / STOOLS]

	Before treatment	After treatment
Niram		
Irugal		
Ilagal		
Others		

VIII. MOOTHIRAM [URINE EXAMINATION]
NEERKKURI:

Neerkkuri	Before treatment	After treatment
Niram		
Manam		
Edai		
Nurai		
Enjal		

NEIKKURI:

Neikkuri	Before treatment	After treatment
Aravananeedathu/ Snake like pattern		
Azhipolparaviyathu Annular/Ringedpattern		
Muththothuninrathu Pearlbeadepattern		
Other patterns		

11. MANIKADAINOOL (WRIST CIRCUMETRIC SIGN):

BEFORE TREATMENT Finger Breadths :

12. CLINICAL EXAMINATION:

CLINICAL EXAMINATION OF SKIN :

1.Site

2.Shape: Coin shape ☐ Irregular ☐ Dispersed ☐

3. Erythema: Present ☐ Absent ☐

4. Macule : ☐ ☐

5. Papule : ☐ ☐

6. Pustule : ☐ ☐

7. Itching: No ☐ Mild ☐ Moderate ☐ Severe ☐

8. Scaling: Mild ☐ Moderate ☐ Severe ☐

9.Fissures : Present ☐ Absent ☐

10.Oozing: No ☐ Mild ☐ Moderate ☐ Severe ☐

11.Lichenification : Present ☐ Absent ☐

12. Auspitz sign : Present ☐ Absent ☐

13. Koebner's phenomenon: Present ☐ Absent ☐

14. Candle grease sign: Present ☐ Absent ☐

EXAMINATION OF NAILS:

1. Pitting: Present ☐ Absent ☐
2. Thickening: Present ☐ Absent ☐
3. Collection of Hyperkeratotic debris: Present ☐ Absent ☐
4. Separation of distal portion of nail: Present ☐ Absent ☐

EXAMINATION OF JOINTS:

	YES	NO
Joint Involvement	☐	☐

PSORIASIS AREA AND SEVERITY INDEX (PASI)

A Psoriasis Area and Severity Index (PASI) is a quantitative rating scale for measuring the severity of psoriatic lesions based on area coverage and plaque appearance

Erythema/ Thickness/Scaling-Rating score	**Area Scoring**
0 - None	0-Nil
1- Slight	1-1-9%
2- Moderate	2- 10%-29%
3-Severe	3-30%-49%
4-Very severe	4-50%-69%
	5-70%-89%
	6-90%-100%

PASI CALCULATION

Plaque Characteristic	**Rating Score**	**Body region and weighting factor**			
		Head	**Upper Limbs**	**Trunk**	**Lower Limbs**
Erythema	**0 = None**				
Thickness	**1 = Slight**				
	2 = Moderate				
Scaling	**3 = Severe**				
	4 = Very Severe				
Totals					
Weighting Factor		**x 0.1**	**x 0.2**	**x 0.3**	**x 0.4**

Surface area totals					
Degree of involvement as % for each body region affected (score each region between 0 and 6)	**0 = None**				
	1 = 1-9%				
	2 = 10-29%				
	3 = 30-49%				
	4 = 50-69%				
	5 = 70-89%				
	6 = 90-100%				
Surface area totals x % involvement totals Sum Scores above =					

- Add together each of Erythema/Thickness/Scaling scores for each of the body regions to give 4 separate sub totals A1, A2, A3 and A4
- Multiply each subtotal by amount of body surface area represented by that region i.e. A1 x 0.1 for head, A2 x 0.2 for upper limbs, A3 x 0.3 for trunk, A4 x 0.4 for lower limbs to give a value B1, B2, B3 and B4 for each body region respectively.A1 x 0.1=B1; A2 x 0.2=B2; A3 x0.3=B3; A4 x 0.4=B4
- For each body region multiply subtotal B1, B2, B3 and B4 by the score(0-6) of the % of body region involved to give 4 sub totals C1, C2, C3 and C4
- The patient's PASI score is the sum of C1+C2+C3+C4

Date:
Station:
Signature of the Investigator:
Signature of the Lecturer: **Signature of the HOD**

PROGRESS OF TREATMENT

PASI SCORE	**1st day**		**8th day**	**15thday**	**22ndday**	**29thday**	**36th day**	**41thday**	**48thday**

DERMATOLOGY LIFE QUALITY INDEX (DLQI)

Hospital No: é é é é é é é é é é é é é . **Date:** é é é é é é é é .

Name: é é é é é é é é é é é é é é . **Score:** é é é é é é é é .

Address: é é é é é é é é é é é é é . **Diagnosis:** é é é é é é é é .

é é é é é é é é é é é é é é .

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick (✓) one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒		
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒		
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒ ❒	Not relevant	❒
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒ ❒ ❒		
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒

Please check you have answered EVERY question. Thank you.

DERMATOLOGY LIFE QUALITY INDEX (DLQI) - INSTRUCTIONS FOR USE

The Dermatology Life Quality Index questionnaire is designed for use in adults, i.e. patients over the age of 16. It is self explanatory and can be simply handed to the patient who is asked to fill it in without the need for detailed explanation. It is usually completed in one or two minutes.

SCORING

The scoring of each question is as follows:

Very much	scored 3
A lot	scored 2
A little	scored 1
Not at all	scored 0
Not relevant	scored 0
Question 7, óprevented work or studyingô	scored 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

HOW TO INTERPRET MEANING OF DLQI SCORES

0 ï 1	no effect at all on patient's life
2 ï 5	small effect on patient's life
6 ï 10	moderate effect on patient's life
11 ï 20	very large effect on patient's life
21 ï 30	extremely large effect on patient's life

REFERENCES

Finlay AY and Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; **19:**210-216.

Basra MK, Fenech R, Gatt RM, Salek MS and Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. *Br J Dermatol* 2008; **159:**997-1035.

Hongbo Y, Thomas CL, Harrison MA, Salek MS and Finlay AY. Translating the science of quality of life into practice: What do dermatology life quality index scores mean? *J Invest Dermatol* 2005; **125:**659-64.

There is more information about the DLQI, including over 85 translations, at www.dermatology.org.uk. The DLQI is copyright but may be used without seeking permission by clinicians for routine clinical purposes. For other purposes, please contact the copyright owners.

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Principal Investigator: Dr.K.ARCHANA
CTRI REG.NO : CTRI/2018/07/015115

1. SERIAL NO:

2. OP /IP NO:

3. NAME:
4. AGE/GENDER:

FORM - LABORATORY INVESTIGATIONS

BLOOD INVESTIGATIONS		NORMAL VALUES	BEFORE TMT (DATE)	AFTER TMT (DATE)
Hb (gm/dl)		M:12-15 W:11.5-12		
T.WBC (cells/cu.mm)		4000-11000		
DIFFERENTIAL COUNT (%)	Polymorphs	40-75		
	Lymphocytes	20-40		
	Monocytes	2-10		
	Eosinophils	1-6		
	Basophils	0-1		
T.RBC (million cells / cu.mm)		M:4.0-5.5 W:3.5-4.5		
ESR (mm/hour)	½ hr.	M:6-12 W:7-18		
	1 hr.			
Blood glucose (mg/dl)	Fasting	70-110		
	PP	80-140		
	Random	80-120		
RFT (mg/dl)	Blood urea	16-50		

	Serum Creatinine	**0.6-1.2**		
LFT (mg/dl)	**Total bilirubin**	**0.2-1.2**		
	Direct bilirubin	**0.1-1.2**		
	Indirect bilirubin	**0.2-0.7**		
	SGOT	**0-40**		
	SGPT	**0-35**		
	Alkaline phosphatise	**80-290**		

URINE INVESTIGATION	**BEFORE TMT(DATE)**	**AFTER TMT (DATE)**
Albumin		
Fasting sugar		
PP sugar		
Deposits		

Date:

Station:

Signature of the Investigator:

Signature of the Lecturer: **Signature of the HOD**

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CTRI REG.NO : CTRI/2018/07/015115

FORM – DRUG COMPLIANCE FORM

STUDY NO: **OP / IP NO:**

NAME: **AGE / GENDER:**

INTERNAL DRUG

On 1st day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 8th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 15th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 22th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 29th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 36th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 42th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)
On 48th day-Date:	Drugs issued:	(Gms)	Drugs returned:	(Gms)

EXTERNAL DRUG

On 1st day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 8th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 15th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 22th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 29th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 36th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 42th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)
On 48th day-Date:	Drugs issued:	(ml)	Drugs returned:	(ml)

Day	Date	Morning	Evening	Day	Date	Morning	Evening
Day 1				Day25			
Day2				Day26			
Day3				Day27			
Day4				Day28			
Day5				Day29			
Day6				Day30			
Day7				Day31			
Day8				Day32			
Day9				Day33			
Day10				Day34			
Day11				Day35			
Day12				Day36			
Day13				Day37			
Day14				Day38			
Day15				Day39			
Day16				Day40			
Day17				Day41			
Day18				Day42			
Day19				Day43			
Day20				Day44			
Day21				Day45			
Day22				Day46			
Day23				Day47			
Day24				Day48			

Date:

Station:

Signature of the Investigator:

Signature of the Lecturer: **Signature of the HOD**

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Ctri Reg.No : CTRI/2018/07/015115

FORM -DIETARY ADVICE FORM

1.SERIAL NO: **2. OP /IP NO:**

3. NAME: **4. AGE/GENDER:**

சேர்க்கக்கூடிய உணவுகள் (DO)	தவிர்க்கக்கூடிய உணவுகள் (DON'T)
இனிப்பு கோவை (Ivy gourd)	அகத்திக்கீரை(Sesban green)
வெள்ளரிப் பிஞ்சு (Baby cucumber)	சிறுகீரை(Chirukiirai)
கத்தரிப் பிஞ்சு (Baby brinjal)	வெற்றிலை (Betal leaf)
அவரைப் பிஞ்சு (Lablab bean)	கொத்தவரை (Cluster bean)
தேங்காய் (Coconut)	மரவள்ளிக்கிழங்கு(Cassava tapioca)
பறங்கிகாய் (Cucurbita maxima)	சேப்பங்கிழங்கு (Colocasia root)
முள்ளங்கி (Radish)	சக்கரவள்ளிக்கிழங்கு (Chakkaravalli)
வெண்டைக்காய் (Lady's finger)	கருணைகிழங்கு (Elephant yam)
வாழைப்பூ (Plantain flower)	வாழைக்காய் (Raw banana)
வாழைத்தண்டு(Plantain stem)	காளான் (Mushroom)
கேரட் (Carrot)	பாகற்காய் (Bitter gourad)
கிச்சிலி (Kolunji naraththai-Tangerine)	பீர்க்கங்காய் (Ribbed luffa)
உருளைக்கிழங்கு (Potato)	புளி (Tamarind fruit)
தடியன்காய் (White pumpkin)	காலிப்பிளவர் (Cauliflower)
சுரைக்காய் (Bitter bottle gourd)	கொத்துமல்லிவிதை (Coriander seed)
சுண்டை (Unarmed night shade)	வரகு அரிசி (Kodo millet)

தக்காளி (Cape gooseberry) மணத்தக்காளி (Black night shade green) அரைகீரை (Araikkirai) கரிசாலை (Trailling eclipta) முளைகீரை (Mulaikiirai) பசலைக்கீரை (Portulaca quadrifida.Linn) புதினா (Marsh mint) குப்பைமேனி (Indian acalypha green) சிறு குறிஞ்சான் (Periploca of the woods green) பொன்னாங்காணி (Sessile plant) வல்லாரை (Indian pennywort) தூதுவளை (Climbing brinjal green) முடக்கற்றான் கீரை (Ballon-vine) முருங்கை கீரை,பிஞ்சு காய் (Drumstick) கொத்துமல்லி கீரை,விதை (Coriander seed) பூண்டு (Garlic) இஞ்சி (Ginger) உளுந்து (Black gram) பாசிபயறு (Green gram) பருத்திவிதை (Indian cotton plant seed) பார்லி(Barley) துவரை (Dholl) சவ்வரிசி (Sago) ஏலம் (Cardamom seed) கசகசா (Opium poppy) மிளகு (Pepper) வெந்தயம் (Fenugreek) கடுகு (Black mustard seed) சீரகம் (Cumin seed) சுக்கு (Dried ginger) முந்திரி பழம்,பருப்பு (Fruit,Cashew nut) இலந்தைப்பழம் (Ber fruit) அத்தி (Fig) ஆப்பிள் (Apple) பேரீச்சு (Date palm) எலுமிச்சை (Lemon) சப்போட்டா (Sapota)	பச்சரிசி (Raw rice) கோதுமை (Wheat) எள் (Sesame seed,oil) வேர்கடலை (Pea nut) கடலை (Bengal gram) கம்பு (Pear millet) கேழ்வரகு (Ragi) காராமணி (Cow gram) சோளம் (Great millet) கொள்ளு (Horse gram) தினை (Italian millet) சாமை(Little millet) தட்டபயறு (Flat bean) மொச்சைப்பயறு (Lablab purpureus.Linn) காப்பிக்கொட்டை (Coffee) களிப்பாக்கு (Areca nut) அருநெல்லி (Countrg goose berry) அன்னாசிபழம் (Pineapple) கொய்யா(Guava) சீத்தாபழம் (Custard apple) பலாபழம் (Jack fruit) மாம்பழம் (Mango) பனைபழம் (Palmyra palm fruit) மாடு கறி (Beaf) கருவாடு (Dry fish) மீன் (Fish) நண்டு (Crab) நத்தை(Snail) இறால்(Prawn) கோழிக்கறி (Chicken)

நாவல் பழம் (Jambul) நெல்லி (Indian gooseberry) பப்பாளி(Papaya) திராட்சை (Grapes) மங்குஸ்தான் (Mangosteen) மாதுளை (Pomagranate) விளம்பழம் (Wood apple) கரும்பு (Sugarcane) அறுகம்புல் (Barmuda grass juice) நன்னாரி (Indian sarsaparilla sarbath) செம்பரத்தை (Hibiscus rosa sinensis Tea) துளசி (Holy basil water) வெள்ளாடு பால் (Goat milk) வெள்ளாடு கறி Mutton மோர் (Butter milk) தயிர் (Curd) வெண்ணெய் (Butter) நெய் (Ghee) தேங்காய் எண்ணெய் (Coconut oil) பாசிபயறு மாவு (Green gram powder) -குளிக்க-Bath	முட்டை(Egg) எருமைப்பால் (Buffalo milk) செம்மறியாடுப் பால்(Sheep milk) செம்மறியாடுக் கறி(Sheep) பன்றிக்கறி (Pig) மூக்கிரட்டை (Boerhavia diffusa) ஊறுகாய் (Pickle) புளிப்பு தயிர் (Sour curd) புளிப்பு மோர் (Sour buttermilk) பெண்போகம்(Intercourse) புகையிலை (Tobacco) புகைப்பிடித்தல்(Smoking) மது அருந்துதல்(Alcohol) சீகைக்காய் (Acacia concinna) -குளிக்க-Bath.

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF SIRAPPU MARUTHUVAM

PRE CLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM*** (EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU).

Principal Investigator: Dr.K.ARCHANA
CTRI REG.NO : CTRI/2018/07/015115

FORM - WITHDRAWAL FORM

1. SERIAL NO OF THE CASE: ……

2. OP / IP NO: .....

3. NAME: ……

4.AGE: ……

5.GENDER:.....

6. DATE OF TRIAL COMMENCEMENT: ……...

7. DATE OF WITHDRAWAL FROM TRIAL: ……..

8. REASONS FOR WITHDRAWAL:

Reluctant to continue the study Yes/ No

Poor patient compliance &defaulters Yes/ No

Increase in severity of symptoms Yes/ No

Date:

Station:

Signature of the Investigator:

Signature of the Lecturer: Signature of the HOD

NATIONAL INSTITUTE OF SIDDHA
AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF SIRAPPU MARUTHUVAM

PRE CLINICAL AND COMPARATIVE CLINICAL TRIAL OF SIDDHA DRUGS ***PARANGIPATTAI KUDINEER*** (INTERNALLY) AND ***SIVAPPU THYLAM (***EXTERNALLY) IN THE TREATMENT OF ***KALANJAGAPADAI*** (PSORIASIS) WITH AND WITHOUT YOGAM THERAPY (AGATHAVAM ETTU).

Principal Investigator: Dr.K.ARCHANA
CTRI REG.NO : CTRI/2018/07/015115

FORM – ADVERSE REACTION FORM / PHARMACO VIGILANCE FORM

SERIAL NO:

OP/IP NO:

NAME: **AGE:** **GENDER:**

DATE OF TRIAL COMMENCEMENT:

DATE OF THE ADVERSE REACTION OCCUR:

DESCRIPTION OF ADVERSE REACTION:

Date:

Station:

Signature of the Investigator:

Signature of the Lecturer: **Signature of the HOD**

NATIONAL PHARMACOVIGILANCE PROGRAMME FOR SIDDHA DRUGS

Reporting Form for Suspected Adverse Reactions to Siddha Drugs

Please note: i. All consumers / patients and reporters information will remain confidential.

ii. It is requested to report all suspected reactions to the concerned, even if it does not have complete data, as soon as possible.

Peripheral Center code: State:

1. Patient consumer identification (please complete or tick boxes below as appropriate)

Name	Father name	Patient / Record No.
Ethnicity	Occupation	
Address Village / Town Post / Via District / State		Date of Birth / Age:
		Sex: Male / Female Weight : Degam:

2. Description of the suspected Adverse Reactions (please complete boxes below)

Date and time of initial observation		Season:
Description of reaction		Geographical area:

. List of all medicines Formulations including drugs of other systems used by the patient during the reporting period:

Medicine	Daily dose	Route of administration Vehicle – Ad uvant	Date		Diagnosis for which medicine taken
			Starting	Stopped	
Siddha					
Any other system of medicines					

. rief details of the Siddha Medicine which seems to be toxic :

Details	Drug – 1	Drug – 2	Drug - 3
a) Name of the medicine			
b) Manufacturing unit and batch No. and date			
c) Expiry date			
d) Purchased and obtained from			
e) Composition of the formulation / Part of the drug used			

b) Dietary Restrictions if any
c) Whether the drug is consumed under Institutionally qualified medical supervision or used as self medication.
d) Any other relevant information.

5. Treatment provided for adverse reaction:

. The result of the adverse reaction side effect untoward effects (please complete the boxes below)

Recovered:	Not recovered:	Unknown:	Fatal:	If Fatal Date of death:
Severe: Yes / No.	Reaction abated after drug stopped or dose reduced:			
	Reaction reappeared after re introduction:			

Was the patient admitted to hospital? If yes, give name and address of hospital	

. Any laboratory investigations done to evaluate other possibilities If Yes specify:

. Whether the patient is suffering with any chronic disorders
Hepatic Renal Cardiac Diabetes Malnutrition

Any Others

9. H O previous allergies Drug reactions:

1 . Other illness (please describe):

11. Identification of the reporter:

Type (please tick): Nurse / Doctor / Pharmacist / Health worker / Patient / Attendant / Manufacturer / Distributor / Supplier / Any others (please specify)
Name:

Address:
Telephone E – mail if any :

Signature of the reporter: **Date:**

Please send the completed form to:

Name & address of the RRC-ASU / PPC-ASU

The Director
National Institute of Siddha,
(Pharmacovigilance Regional Centre For Siddha Medicine),
Tambaram Sanatorium, Chennai-600 047.
☏ (O) 044-22381314 Fax : 044 – 22381314
Website : www.nischennai.org
Email: nischennaisiddha@yahoo.co.in

* *

This filled-in ADR report may be sent within one month of observation /occurrence of ADR

Who Can Report

⇒ Any Health care professionals like Siddha Doctors / Nurses / Siddha Pharmacists / Patients etc.

What to Report

⇒ All reactions, Drug interactions,

Confidentiality

⇒ The patient's identity will be held in strict confidence and protected to the fullest extent.

⇒ Submission of report will be taken up for remedial measures only not for legal claim

Date :

Station:

Signature of the Investigator:

Signature of the Lecturer: Signature of the HOD

NATIONAL INSTITUTE OF SIDDHA
राष्ट्रीय सिद्ध संसथान -
Ministry of AYUSH - आयुष मंत्रालय
GOVERNMENT OF INDIA-भारत सरकार
TAMBARAM SANATORIUM, CHENNAI -600 047 -ताम्बरम सनटोरियम चेन्नई -600 047
फ़ोन\Tele : 044-22411611 फैक्स\Fax : 22381314
ईमेल: nischennaisiddha@yahoo.co.in वेब :www.nischennai.org

F.No.NIS/6-20/Res/IEC/17-18 Date: 28-12-2017

CERTIFICATE

Address of Ethics Committee: National Institute of Siddha, Tambaram Sanatorium, Chennai-600047, Tamil Nadu, India	
Principal Investigator: Dr.K.Archana, M.D(S) – II year, Department of Sirappu Maruthuvam - Dissertation – Reg.No.	
Protocol title: Pre clinical and Comparative clinical trial of Siddha drugs ***Parangipattai kudineer*** internally and ***Sivappu thylam*** externally in the treatment of ***Kalanjagapadai*** (Psoriasis) with and without Yogam therapy (Agathavam Ettu).	
Documents filed	1) Protocol, 2) Data Collection forms 3) Patient Information Sheet 4) Consent form 5) SAE(Pharmacovigilance)
Clinical trial Protocol (others – Specify)	**Yes**
Informed consent documents	**Yes**
Any other documents	**-**
Date of IEC approval & its number	**NIS/13-IEC/2017-1-08/ 22-11-2017**

We approve the trial to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study, Review periodically, any SAE occurring in the course of the study, any changes in the protocol and submission of final report

Chairman

NATIONAL INSTITUTE OF SIDDHA ★ CHENNAI 600 047

Member Secretary 29/12/17

CERTIFICATE

This is certify that the project title**To evaluate the Safety profile of*"Parangipattai Kudineer"* - *Acute &Subacute toxicity study*** hasbeen approved by the IAEC. Total No. of animals Sanctioned: 46 Rats (20 M + 26 F). IAEC Approval No: NIS/IAEC VI /2404/2018/09

Prof.Dr.V.Banumathi

Chairman IAEC:

Prof.Dr.K.Nachimuthu

Name of CPCSEA nominee:

Signature with date:

Chairman/Member Secretary of IAEC: CPCSEA nominee:

(Kindly make sure that minutes of the meeting duly signed by all the participants are maintained by Office)

Name of the investigator : Dr.K.Archana, II year PG scholar

Name of the department : Sirappu Maruthuvam

Name of the guide : Dr.M.V.Mahadevan M.D (s)
Lecturer,
Dept.of Sirappu Maruthuvam,
National Institute of Siddha.

CERTIFICATE

सत्यमेव जयते
Ministry of AYUSH

NATIONAL INSTITUTE OF SIDDHA

Ministry of AYUSH, Government of India

Tambaram Sanatorium, Chennai - 600 047.

WORKSHOP ON
RESEARCH METHODOLOGY & BIOSTATISTICS

This is to certify that

Dr. K. ARCHANA

has participated in the above Workshop held from 16.04.2018 to 20.04.2018 conducted by the Dept. of Noi Naadal, at National Institute of Siddha, Tambaram Sanatorium, Chennai-600 047.

Dr. G.J. Christian
Coordinator
HoD, Dept. of Noi Naadal,
National Institute of Siddha

Prof.Dr.V.Banumathi
Director,
National Institute of Siddha
Chennai – 600 047.

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 600047

BOTANICAL CERTIFICATE

Certified that the following plant drugs used in the Siddha formulation **"Parangipattai Kudineer"** (Internal) and **"Sivappu Thailam"** (External) taken up for Post Graduation Dissertation studies by **Dr.K.Archana** M.D.(S). II year. Department of Sirappu Maruthuvam, 2018. are identified through Visual inspection. Experience. Education & Training. Organoleptic characters. Morphology and Taxonomical methods as

Smilax china Linn. (Liliaceae). Root

Picrorhiza kurroa Royle ex Benth. (Scrophulariaceae). Root

Rubia cordifolia Linn.(Rubiaceae). Root

Coscinium fenestratum (Gaertn.) Colebr. (Menispermaceae). Stem

Terminalia chebula Retz. (Combretaceae). Fruit

Terminalia belerica Roxb. (Combretaceae). Fruit

Acorus calamus Linn. (Araceae). Rhizome

Azadirachta indica A. Juss. (Meliaceae). Stem bark

Pimpinella anisum Linn. (Apiaceae). Fruit

Tinospora cordifolia (Willd.) Meirs (Menispermaceae). Stem

Pongamia pinnata (Linn.) Merr. (Fabaceae). Root

Hemidesmus indicus R.Br. (Periplocaceae). Root

Vateria indica Linn. (Dipterocarpaceae). Oleoresin

Dioscorea purpurea Roxb. (Dioscoreaceae). Stem

Cinnamomum verum Presl. (Lauraceae). Bark

Cocos nucifera Linn. (Arecaceae). Oil.

MEDICINAL BOTANY CHENNAI 600 047 National Institute of Siddha

Certificate No: NISMB3192018

Date: 09-03-18

Authorized Signatory

Dr. D. ARAVIND, M.D.(s),M.Sc.,
Assistant Professor
Department of Medicinal Botany
National Institute of Siddha
Chennai - 600 047, INDIA

Clinical Trial Details (PDF Generation Date :- Thu, 18 Jul 2019 08:02:53 GMT)

CTRI Number	CTRI/2018/07/015115 [Registered on: 30/07/2018] - **Trial Registered Prospectively**
Last Modified On	26/07/2018
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Drug Siddha Other (Specify) [Yogam]
Study Design	Single Arm Trial
Public Title of Study	“Clinical trial of Siddha drugs Parangipattai Kudineer (Internally) and Sivappu Thylam (Externally) in the treatment of Kalanjaga Padai (Psoriasis) with and without Yogam therapy”
Scientific Title of Study	“Preclinical and comparative clinical trial of Siddha drugs Parangipattai Kudineer (Internally) and Sivappu Thylam (Externally) in the treatment of Kalanjagapadai (Psoriasis) with and without Yogam therapy (Agathavam Ettu)”

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Dr K Archana
Designation	MD Siddha
Affiliation	Ayothidass pandithar hospital, National Institute of Siddha
Address	Department of Sirappu Maruthuvam, Ayothidass pandithar hospital, National Institute of Siddha, Tambaram Sanatorium, Chennai Kancheepuram TAMIL NADU 600047 India
Phone	8675544027
Fax	
Email	licaachu@gmail.com

Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Dr N J Muthukumar
Designation	Head of the Department
Affiliation	Ayothidass pandithar hospital, National Institute of Siddha
Address	Department of Sirappu Maruthuvam, Ayothidass pandithar hospital, National Institute of Siddha, Tambaram Sanatorium, Chennai Kancheepuram TAMIL NADU 600047 India
Phone	9444206843
Fax	
Email	njmuthu@hotmail.com

Details Contact Person (Public Query)

Details Contact Person (Public Query)	
Name	Dr M V Mahadevan
Designation	Lecturer
Affiliation	Ayothidass pandithar hospital, National Institute of Siddha
Address	Department of Sirappu Maruthuvam, Ayothidass pandithar hospital, National Institute of Siddha, Tambaram Sanatorium, Chennai Kancheepuram TAMIL NADU

	600047 India
Phone	9840417565
Fax	
Email	mahasiddha2009@gmail.com

Source of Monetary or Material Support

Source of Monetary or Material Support
> Self (K Archana PG Scholar National Institute of Siddha Tambaram sanatorium chennai 47

Primary Sponsor

Primary Sponsor Details	
Name	Dr K Archana
Address	Ayothidass pandithar hospital, National Institute of Siddha, Tambaram Sanatorium, Chennai
Type of Sponsor	Other [(Research Student)]

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr K Archana	National Institute of Siddha	Department of Sirappu Maruthuvam Ayothidass pandithar hospital National Institute of Siddha Tambaram sanatorium Chennai Kancheepuram Tamil Nadu Chennai TAMIL NADU	8675544027 licaachu@gmail.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
The Institutional Ethical Committee National Institute of Siddha Chennai- 47 Tamil Nadu India	Approved	22/11/2017	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Patients	Patients with symptoms of dry erythematous macules with silvery scales without any structural changes in any part of the body

Intervention / Comparator Agent

Type	Name	Details
Intervention	Parangipattai Kudineer (Internally) and Sivappu Thylam (Externally)	Parangipattai Kudineer is a polyherbal formulation in a dosage of 30ml internally,Three times a day and Sivappu Thylam applied externally in the affected areas for 48 days.
Comparator Agent	NA	NA

Inclusion Criteria

Inclusion Criteria

Age From	20.00 Year(s)
Age To	65.00 Year(s)
Gender	Both
Details	1)History of Non Insulin Dependent Diabetes Mellitus 2)Dry erythematous macules with silvery scaly lesion without any structural changes in any part of the body. 3) Itching 4)Erythema 5)Scaling 6)Auspitz sign + 7)Candle crease sign + 8)Willing to give specimen of blood for the investigation whenever required. 9)Willing to take photograph 10)Willing to participate in trial and signing consent by fulfilling the condition of Proforma.

Exclusion Criteria

Exclusion Criteria	
Details	1.History of Insulin Dependent Diabetes Mellitus 2.Pregnancy and lactation 3.History of Psoriasis with evidence of any other skin disease or Evidences of secondary infection in the lesions. 4.History of Psoriatic arthropathy 5.History of Cardiac diseases 6.History of Hansen's disease 7.History of any other chronic illness

Method of Generating Random Sequence	Not Applicable
Method of Concealment	Not Applicable
Blinding/Masking	Not Applicable

Primary Outcome

Outcome	Timepoints
Efficacy of the trial drug measured by PASI Score.	1-48 DAYS

Secondary Outcome

Outcome	Timepoints
1.To study the Siddha diagnostic methods such as Envagai thervu and Manikkadai Nool as complementary measures for diagnosis in Kalanjaga padai patients. 2.To carry out the biochemical analysis of trail medicine Parangipattai kudineer (Internally) 3.To evaluate the toxicity study of trail medicine Parangipattai kudineer (Internally)	1-48 DAYS

Target Sample Size	**Total Sample Size=**40 **Sample Size from India=**40 **Final Enrollment numbers achieved (Total)=**Applicable only for Completed/Terminated trials **Final Enrollment numbers achieved (India)=**Applicable only for Completed/Terminated trials
Phase of Trial	Phase 2
Date of First Enrollment (India)	25/09/2018
Date of First Enrollment (Global)	No Date Specified

Estimated Duration of Trial	**Years=**1 **Months=**6 **Days=**0
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Not Yet Recruiting
Publication Details	Archana.K.,et al , Polyherbal Siddha Formulation Parangipattai Kudineer : A Review, ejbps , 2018, Volume 5, Issue 6, 196-201.
Brief Summary	Siddhars identified numerous number of herbal for treating Kalanjagapadai (Psoriasis). One such Siddha herbal formulation **"Parangipattai Kudineer" (Internal) and "Sivappu Thylam" (External)** mentioned in "Pharmacopoeia of hospital of Indian medicine" which is said to be cost effective, efficacious and simple formulation. This formulation has not undergone any a preclinical study and clinical study with yogam so far.The ingredients of *Parangipattai kudineer* (Internally) are Parangipattai *(Smilax china Linn.)*,Kadugu Rohini *(Picrorhiza kurroa Royle)*,Manjitti *(Rubia cordifolia Linn.)*, Mara Manjal *(Coscinium fenestratum Colebr.)*,Kadukkai *(Terminalia chebula Retz.)*,Thandrikai *(Terminalia bellaricaRoxb.)*,Vasambu *(Acorus calamus Linn)*,Sombu *(Pimpinella anisum Linn.)*,Veppampattai *(Azadirachta indica A.Juss.)*,Seendhil *(Tinospora cordifolia Miers.)* are also having Antipsoriatic, Immunomodulator, Anti-Inflammatory, Antifungal, Antimicrobial, Antianalgesic. So that I hope this medicine will be effective in the treatment of Kalanjagapadai (Psoriasis). Therefore I have selected the drug for clinical study.

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